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Vol. XXXV TOPEKA, KANSAS, MAY, 1934 No. 5

ORIGINAL ARTICLES

THE PATHOLOGY OF HYPERTENSION

H. R. Wahl, M.D.,* and
W. C. Curphey, M.D.†

The nature and causes of hypertension and its relation to renal disorders remains a mystery in spite of years of investigation. Studies of the cellular changes occurring in well differentiated types of high blood pressure may contribute eventually to the elucidation of this puzzling condition. It is for this reason that a microscopic study of the tissues from 92 selected cases of fatal hypertension was made and forms the basis of this communication.

All but two cases included in this study had a persistent blood pressure of 180 or over. They may be classified into four main types, based on the outstanding clinical symptoms and signs immediately prior to the fatal termination, viz, cardiac, apoplectic, uremic and convulsive. Of the 92 cases, 14 were of the uncomplicated cardiac type while 21 were similar but complicated with evidences of severe renal damage. The apoplectic group included 31 cases of which 22 were uncomplicated examples of cerebral hemorrhage while nine showed evidences of severe renal failure. There were 18 cases of uremic death included in this series. In addition there were eight instances of peculiar vascular crises with prominent convulsive symptoms, high blood pressure and extensive kidney disease. Several cases of toxemias of pregnancy were included in this group. In other words, the last two groups presented evidences of extensive renal failure while similar kidney damage was evident in most of the cardiac (60 per cent) group and in the apoplectic group (70 per cent). From this analysis it is evident that of the 92 cases, 69 or 75 per cent showed abnormal urinary or blood findings indicative of renal damage.

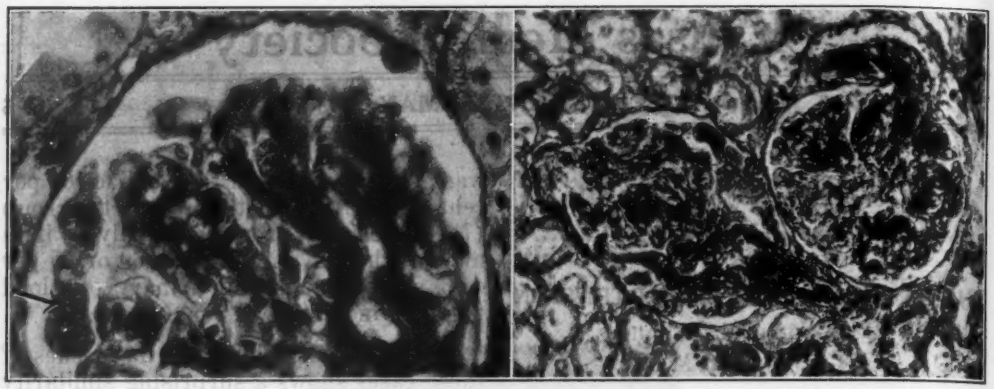
The microscopic study of the tissues of these cases shows a surprising similarity in the four groups though minor differences in the degree of changes may occur. The vascular apparatus shows the chief changes and they may be separated into two groups, one in which the lesions are chiefly glomerular and the other involving the small arterioles of various viscera such as the pancreas, kidney, spleen and adrenal glands. The clinical differences were not associated with corresponding anatomical distinctions. The changes were essentially vascular and varied only in degree. The same glomerular lesions were seen in the cardiac as well as the apoplectic cases, and the same alterations in the arterioles in the uremic as in the convulsive series.

The characteristic glomerular changes were the following: proliferation and swelling of the endothelial and epithelial cells of the tuft, hyaline droplet degeneration in the epithelial cells of the glomerular tuft, swelling of the basement membrane, infiltration with leukocytes and fibrin and crescent formation through proliferation of the capsular epithelial cells.

The arteriolar changes consist in swelling and proliferation of the endothelial cells, swelling and alteration in the staining of the internal limiting membrane and necrosis and leukocytic infiltration extending from the wall into the surrounding tissue (necrosing arteritis). Frequently a thick hyaline collar apparently encloses and almost occludes the lumen of the vessel. Often the markedly thickened walls of the smaller arteries are seen to

*Dean of the School of Medicine and Professor of Pathology.
†Department of Pathology.

GLOMERULAR CHANGES IN HYPERTENSION



A. Part of tuft x450. Note thickening of the basement membrane and hyaline droplets in the epithelial cells of the tuft.

B. Note the diffuse Fibrosis and thickening of the basement membrane, also hyaline changes in the arterioles. x 150.

be due to increase in collaginous fibrous tissue with even atrophy of the smooth muscle cells. This is strikingly illustrated by means of Masson's trichrome stain. These arteriolar changes are quite prominent in the afferent artery of the glomerulus especially in the cases of known glomerulonephritis such as in the uremic group. The thick hyaline collars were particularly prominent in the arterioles of the spleen, pancreas, adrenals and even in the meninges as well as in the kidneys in the nephrosclerotic cases.

Since atherosclerotic changes in the large and medium sized arteries have no constant influence on the blood pressure, they have not been included in this study even though they were present in most of the material studied. Frequently, they are well marked and the blood pressure is normal. The heart was hypertrophied in all of our cases, especially the left ventricle; the valves usually showed no organic changes.

While renal lesions involving the glomeruli and arterioles were almost always present it does not follow that the reverse is true. Advanced renal lesions involving both glomeruli and arterioles may occur without hypertension. One of the cases studied was particularly interesting in this respect. It showed rather advanced glomerular and arteriolar changes of a uremic case and yet in spite of several years careful observation never showed a blood pressure of over 130. This illustrates that there is no constant relation between prolonged hypertension and glomerular and arteriolar lesions and affords support to the theory that another factor, possibly a blood toxin, causes both the anatomical lesions in the glomeruli and arterioles and the elevation of the blood pressure. Furthermore, while it is true that the arteriolar changes were present in the kidneys, pancreas and spleens of all cases of hypertension and a few without it, it is difficult to ascertain whether these changes are the cause or the result of the hypertension. It is more likely that they are both due to a common cause such as methylquanidin.

Another of these cases is of unusual interest, the clinical history being that of typical paroxysmal hypertension associated with the presence of a tumor of the adrenal medulla found at the autopsy. The tumor is known as a paraganglioma and has been reported recently in association with, if not the cause, of attacks of high blood pressure (in this case up to 240 Hg.) The study of the glomeruli and the arterioles in the kidney, spleen and pancreas show the same hyaline changes noted in other cases of hypertension suggesting that they follow rather than precede the hypertension and that the tumor is the cause of the functional disturbance in the vasomotor mechanism.

The convulsive cases deserve special

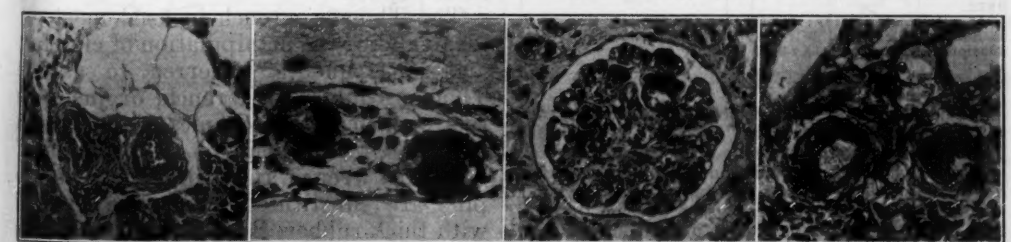
comment. They are often associated with spasmodic contractions of the arterioles which has been observed in studies of the behavior of vessels in the retina. It is quite possible that similar spasms of the cerebral arteries may occur and cause the convulsive seizures associated with hypertension. The glomerular changes and those in the arterioles of these vascular crises and pregnancy toxemias are very similar to those seen in other types of hypertension except that in the arterioles a necrosing arteritis in the meninges as well as in other organs may occur. It is quite probable that the same etiological factor is the basis of these convulsive types of hypertension as the others, only here the arteriolar changes are more acute and more likely to be associated with spasmodic or functional changes.

The study of these cases of hypertension also indicates that there is little difference between the pathogenesis of nephrosclerosis (chronic interstitial nephritis) and glomerulonephritis in both of which the blood pressure is considerably elevated. The main distinction is the predominance of the arteriolar changes in other elements in the kidney while in glomerulonephritis the toxic agent affects the glomeruli tubules and arterioles directly.

The recent experimental results of Goldblatt and others showing the persistent production of hypertension in dogs by gradual mechanical occlusion of the renal arteries is very suggestive in connection with this study. This is comparable to reduction in renal circulation and production of ischemia similar to what would occur with arteriolar and glomerular disease such as was present in most of our cases. It would indicate that simple reduction in renal circulation such as was evident in most of our cases could in itself produce hypertension. On the other hand it does not exclude the presence of a toxic substance causing both a pressor effect on the vasomotor system and characteristic arteriolar and glomerular lesions. There is considerable evidence that persistent elevation of blood pressure will lead to hyalinization of arterioles and basement membrane thickening in the glomeruli but less evidence that these anatomical changes will cause hypertension. This work of Goldblatt, however, gives some basis for a reciprocal reaction.

The theory of Addis of the relation of kidney lesions to hypertension is quite convincing and seems to coincide with the findings in this study. Addis maintains that in addition to the constantly occurring factors which produce arteriosclerosis there is a third independent factor, toxic and irritating in nature, which may not only accelerate the existing vascular lesions and thus damage the kidney, but in many instances affect the organic tissues directly and in the same manner and with the same effect as is observed in glomerulonephritis. Furthermore, this agent may affect groups of arterioles in other organs such as the brain that would lead to a permanent change in the regulatory mechanism of the blood pressure. Again such a toxin may cause a generalized vasoconstriction by its direct irri-

ARTERIOLAR CHANGES



A. Hyaline collars in arterioles of kidney in the uremic type of hypertension. x 450.

B. Hyaline collars in arterioles in the meninges of the brain in a case of cerebral vascular crisis associated with hypertension x 450.

C. Hyaline collars in capillary tuft of glomerulus in a case of essential hypertension. x 250.

D. Hyaline collars in arterioles in pancreas. Same case as B. x 250.

tating effect on the arterioles and thus account for the acute vascular crises such as may occur in eclampsia.

In conclusion, it may be stated that the etiology of hypertension and the cellular changes in the glomeruli and arterioles is apparently the same. It would appear most likely that both are the result of the same common agent. At least this is the most plausible theory in the light of present information. This common agent may in a few cases be a paraganglioma of the adrenal gland which elaborates a toxic substance that is absorbed by the blood and exerts a pressor effect on the vasomotor mechanism. If the action of the common toxic agent persists it produces an anatomical change in the arterioles and glomeruli in sufficient amount to make the hypertension permanent even if the toxic agent disappears.

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USE OF THE THOMAS WRENCH IN THE REDUCTION OF FRACTURES AND DISLOCATIONS.

JAMES B. WEAVER, M.D.*

A very useful instrument for the reduction of certain fractures and dislocations, the merit of which is not generally recognized, is the Thomas wrench. This device is the result of the genius of Hugh Owen Thomas (1834-1891) whose leg splint was so extensively used during the World War and is known wherever fractures are treated. Thomas was the last of a direct line of bone setters of Liverpool, England, which had passed from father to son for seven generations. Incidentally he was the first qualified practitioner of this long line and had to sever his partnership with his father due to the English Medical Act of 1858. About 20 years later a young nephew, Robert Jones, became his associate and was taught the art of manipulative surgery.

While Thomas invented the Thomas wrench, it was his nephew, the late Sir Robert Jones, who popularized its use. Sir Robert is authority for the statement, "Unfortunately the use of this wrench is very imperfectly understood, both in Great Britain and the United States." We once heard one of our beloved teachers, Dr. Royal Whitman, say, "Sir Robert Jones probably knows more about the use of the Thomas wrench than any other person in the world" and quickly, "but I am next." Those who know Dr. Whitman are aware that this was indeed high praise and clearly indicated that Sir Robert was a wizard in the use of the Thomas wrench. We were privileged to confirm this impression a few years later when on a visit to Liverpool.

The Thomas wrench is used most extensively for the manipulation of club feet and is frequently referred to as the Thomas Club Foot Wrench, or just club foot wrench. The mechanics of the wrench is simple. "It is made on the principle of a monkey wrench. Instead of the jaws two pins are substituted which are covered with thick rubber. By twisting the handle of the wrench, these two pins approach or separate from each other." Figure 1

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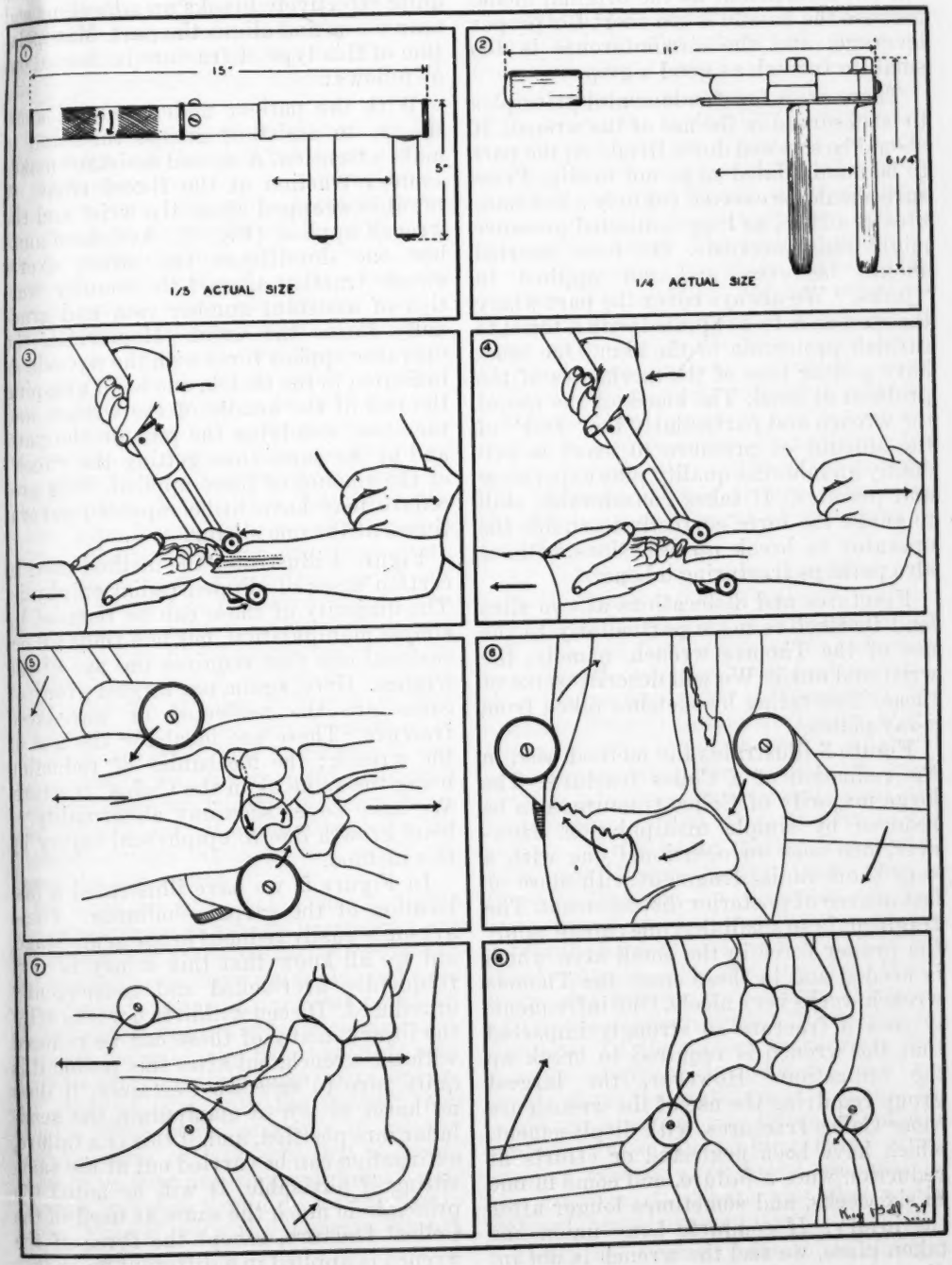
15"
5"
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11"
6 1/4"
1/4 ACTUAL SIZE

shows the original type of wrench. Figure 2 is a type frequently found on the market, but not as efficient as the original model because the handle is too short for proper leverage, and the circumference is too small to furnish as good a grip.

There are a few fundamental principles to be observed in the use of the wrench. It should be screwed down firmly on the part to be manipulated so as not to slip. Pressure should be exerted for only a few minutes at a time, as long continued pressure might cause necrosis. The force exerted should be even and not applied in "jerks." We always cover the part where the wrench is to be applied with a towel to furnish protection to the skin. One must have a clear idea of the mechanics of the problem at hand. The knack of the use of the wrench and particularly the "feel" of the amount of pressure to exert is evidently an inherent quality plus experience and practice. It takes considerable skill to guage the force correctly to enable the operator to break up adhesions without also perhaps fracturing a bone.

Fractures and dislocations at two sites lend themselves more particularly to the use of the Thomas wrench, namely, the wrist and ankle. We will describe some of these, illustrating by sketches taken from *x*-ray plates.

Figure 3 illustrates the method used in the reduction of a Colles fracture. The large majority of Colles fractures can be reduced by simple manipulation. However, one sees an occasional one with a very short radial fragment with more or less degree of posterior displacement. The fragment is so small that one cannot apply the proper force in the small area which is needed and in these cases the Thomas wrench works very nicely. One infrequently sees a fracture so strongly impacted that the wrench is required to break up the impaction. However, the largest group requiring the use of the wrench are those Colles fractures, with displacement, which have been neglected or efforts at reduction were a failure, and come in one to six weeks, and sometimes longer after the injury. If complete bony union has taken place, we feel the wrench is not indicated, in our hands, though Sir Robert had no hesitation in using it in this type. However, if these fractures are still "green", manipulation by the wrench quite effectively breaks up adhesions and scar tissue and aligns the part. Manipulation of this type of fracture is carried out as follows:

With the patient under general anesthesia, an assistant grasps the hand to make extension. A second assistant makes counter traction at the flexed elbow. A towel is wrapped about the wrist and the wrench applied (Fig. 3). Assistant number one dorsiflexes the wrist, exerts steady traction against the counter traction of assistant number two, and gradually flexes the wrist. Meanwhile, the operator applies force with the wrench, as indicated in the sketch, one hand grasping the end of the handle of the wrench and the other steadying the pins on the part, and at the same time getting the "feel" of the amount of force applied. This procedure may have to be repeated several times, at the one sitting.

Figure 4 illustrates the method used in certain cases of slipped radial epiphysis. The majority of these can be reduced by simple manipulation, but one finds an occasional one that requires the use of the wrench. Here, again, our largest group of cases are the neglected or unreduced fracture. These are ideal for the use of the wrench; the mechanics of reduction being the same as in the Colles' fracture. We have never seen any abnormality of bone growth due to epiphyseal injury by this method.

In Figure 5, we have illustrated a dislocation of the carpal semilunar. These are quite easily reduced in the acute stage, but we all know that this injury is very frequently overlooked and consequently unreduced. If seen within two weeks after the injury, many of these can be reduced with the wrench, but after this period it is quite rare to succeed. Certainly, it does no harm to try to manipulate the semilunar into position, and, if this is a failure, extirpation can be carried out at the same sitting if advisable. It will be noted the principle is much the same as used in the Colles' fracture, except the force of the wrench is applied in a different manner.

We have never used the wrench to reduce an acute Pott's fracture. However, it

is very useful in the reduction of the neglected or unreduced ones, to stretch the contracted muscles and tendons, break up scar tissue and adhesions, and to lever the misplaced parts into alignment. The mechanics is obvious from a study of Figure 6.

Posterior marginal fractures of the tibia are quite difficult to reduce or to hold in place once reduction is accomplished. These fractures, therefore, form the largest group of those about the ankles on which we find the use of the wrench indicated. In the difficult acute ones the wrench works quite beautifully, and is very useful in the reduction of the neglected ones. In the chronic cases, we usually find it necessary to insert a Steinman's pin through the os calcis, for better traction to widen the ankle mortise in the longitudinal direction. The mechanics of this procedure is illustrated in Figure 7. This method is usually a failure if the period since injury is three weeks or over.

The conditions so far enumerated are the common ones where the use of the Thomas wrench is indicated. There are, of course, numerous isolated instances where one familiar with the use of the instrument will find it of value. We have illustrated one of these in Figure 8. This is a dislocation of the tarsal scaphoid of one week duration. Due to its size it was impossible to readily grasp the dislocated part. Pressure by thumbs, or heel of hand, was insufficient. Manipulation with the Thomas wrench, as indicated, easily reduced the dislocation.

We have not enumerated case histories and percentages of results because we are not presenting a new method of treatment, but one well over fifty years old, and used frequently by some of our most noted orthopedists. It has never been popularized, perhaps because its use has not been understood. Certainly some operators are far more skillful with the wrench than others. Orthopedic surgeons in general acquire more or less skill, but it would seem to us that any surgeon doing a fair fracture practice would do well to familiarize himself with the Thomas wrench and its use.

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CEREBRAL FAT EMBOLISM

R. W. Kerr, M.D.*

Cerebral fat embolism is frequently overlooked in the study of cases of coma following trauma.

This case is a white male, injured while at work, sustaining a compound comminuted fracture of the left tibia and fibula. There was no evidence of a head injury at the time. Thirty-six hours later the nurse noted he was drowsy and irrational at times. The temperature was elevated, ranging between 101 and 106 degrees. The patient became comatose 72 hours after injury and remained in coma until his death four days later. Physical examination revealed some stiffness of the neck, increased reflexes, petechiae over the chest and upper extremities, also peculiar areas surrounded by hemorrhage were noted in the retinae. The findings did not change except for the development of signs of an extensive bronchopneumonia.

At autopsy, the body had been embalmed. Examination revealed a well developed male, showing a fracture of the left tibia and fibula. Numerous petechiae were found over the chest and extremities. There was some inflammatory reaction in the soft tissues at the site of the fracture. The lungs showed a bilateral bronchopneumonia. On opening the head, nothing abnormal was noted until the brain was sectioned. Here the entire cut surface of the white matter was dotted with small hemorrhages from one to three millimeters in diameter. A few were found in the gray matter of the cerebral and cerebellar cortex and in the basal ganglia. On staining the brain, lungs and kidneys with Sudan III many of the vessels were found filled with fat droplets. In the brain, there were frequently areas of hemorrhage and necrosis about the vessels and in places fat could be seen in the tissue about the occluded vessel. In the lung, many of the smaller vessels were found occluded by the fat droplets. There was also a well defined bronchopneumonia.

Death was evidently due to the changes

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in the brain with the bronchopneumonia playing an important contributory part.

DISCUSSION

Fat embolism may be divided into two types: (1) Pulmonary and (2) general systemic or cerebral. Vance defines fat embolism as, "The condition which occurs when a liquid fat or oil enters the circulatory blood and is transported in globules large enough to obstruct the lumen of blood vessels in different parts of the body." Gauss considers it is always due to trauma and cited three factors he believed should always be present: "(1) Injury to adipose tissue sufficient to liberate free fat into the injured area. (2) The rupture of a certain number of blood vessels, especially veins in the injured area. (3) The establishment of some mechanism which will cause the passage of fat into the open ends of the blood vessels." The first two of these may frequently occur but the latter is much more likely to occur in fractures because here torn vessels may be held open by the bony canals surrounding them and since they cannot collapse the negative pressure tends to draw fat into them. As fat passes into the blood stream, it tends to cause obstruction at the first capillary bed it meets which usually is the lungs. Frequently this occurs 24 to 36 hours after injury or subsequent mobilization. The symptoms at this time are restlessness, rapid feeble pulse, pallor, cyanosis, dyspnea, pulmonary edema and occasionally death occurs at this stage. In these cases, the pulmonary capillaries are usually filled with plugs of fat.

If the fat arrives in the lungs slowly or fat is not too extensive the milder pulmonary symptoms may occur and then gradually clear up as the fat passes through the capillaries or is absorbed. Some of the fat may be taken up by the large phagocytic cells of the lungs and expectorated.

As the fat enters the general circulation, a certain amount may be disposed of in the following ways, according to Gauss: "(1) It may be screened out in the kidneys and some of it passed in the urine; (2) secreted into the gastrointestinal tract by the liver and bile; (3) taken up by phagocytic endothelial cells; emulsified by the blood current and digested by the blood lipases to be taken up again by the tissues."

Of the organs involved by the fat after its entry into the general circulation, the central nervous system causes the most clinical findings. Cases are reported of occlusion of the coronaries with resulting myocardial degeneration; others are reported in which the kidneys are mostly involved even with complete anuria.

Gauss shows that fat emboli may occur in all areas of the central nervous system, are usually associated with edema, hemorrhage, round cell infiltration and in areas focal necrosis showing total destruction of the myelin sheaths and are more abundant in the white matter. He also accounts for the symptoms; first, the irritability and delirium followed by coma as the irritation of the nerve cells, due to loss of blood supply followed by degeneration and necrosis, and suggests the possibility of a diagnosis of delirium tremens if the patient may have been given whisky as a first aid measure following injury.

An interesting case, which recovered, is reported by Corlette. The man received a compound comminuted fracture of the tibia and fibula. Twenty-four hours later he had lung findings with dyspnea and pulmonary edema. These symptoms cleared up in about 24 hours and were followed by convulsions and coma, associated with elevation of temperature, and petechial hemorrhages over the chest and extremities. The cerebral symptoms cleared up in about 72 hours and the patient made an uneventful recovery.

It is interesting to note how closely this history follows that of postoperative cases on which a diagnosis of postoperative reaction or pulmonary embolism is made. The fact that Vance finds operative procedures or any type of trauma to fat, such as bruises or severe jars, sufficient to liberate fat and produce embolism is worthy of consideration in many of these cases. The ophthal-

moscope is of value in the diagnosis of the cerebral type of fat embolism.

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THE REACTION OF TUMORS TO IRRADIATION

FERDINAND C. HELWIG, M.D.*

Considerable confusion exists regarding the determination of the radiosensitivity of tumors, the foremost instance of which is the fact that many physicians have taken for granted that cell differentiation alone determines the reaction of tumors to irradiation therapy. Unfortunately, cell differentiation represents only one of the important factors and in many instances, examples of which will be given, the cell differentiation of a tumor may not only be overshadowed by other findings but may be of no diagnostic assistance whatever.

Expected results of irradiation have often been disappointing due to this and other misinterpretations of the available information in a given case, with the result that confidence in the diagnosis of the degree of sensitivity of tumors to irradiation has often been badly shaken.

Some of the points to be taken into consideration which may lead to an apparent contradiction of the general law that the more embryonal the cell may be, the more sensitive it becomes to the action of radium and x-ray, are the duration of the tumor, the degree of fibrosis, the topographical relationships, the character of the tumor bed, and the gross physical characteristics of the neoplasm. In addition, the factors of secondary infection, previous irradiation and the general nutrition and age of the patient are of utmost importance in determining the response of a tumor to irradiation.

In a general way, it may be said that fibrosis, secondary infection, cachexia, anemia and advancing age all tend to increase the radioresistance of a neoplasm. Since the location of a given tumor in many instances is of considerable importance in judging its radiosensitivity, it becomes at once apparent that every tumor must be considered as a distinct entity located in a certain area where neoplasms of that same class and character are known to respond to irradiation therapy in a fairly uniform manner.

As was previously mentioned, it is impossible to judge the response of a tumor by its cell type alone, and although in a general way anaplasia indicates sensitivity, this generalization is subject to many contradictions. Thus, the very undifferentiated neurogenic sarcomas and melanotic tumors are almost uniformly resistant to irradiation, regardless of their degree of anaplasia. The same holds true for certain undifferentiated epithelial malignancies such as the spindle cell epithelioma of the mouth which is very resistant while the same tumor may be quite sensitive when located posterior to the anterior palatoglossal fold (Stewart). Moreover it has been observed that the more highly differentiated carcinomas of the breast may yield the most marked regressions under irradiation. Likewise, the less anaplastic esophageal carcinomas, the mixed tumors of the parotid gland, and the fascial liposarcomas are more sensitive than the more undifferentiated tumors in these same regions. Such apparently paradoxical conditions exist throughout the whole gamut of tumors, and these illustrations merely suffice to emphasize how important it is to study thoroughly each individual neoplasm from every angle and the necessity of obtaining all of the available information about its life history, gross and microscopic characteristics and clinical associations, before venturing an opinion as to its radiosensitivity.

Furthermore, radioresistance of a given tumor does not necessarily imply that the tumor is incurable, nor does spectacular regression of an extremely radiosensitive growth by any means signify a good ultimate prognosis.

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In making a usable outline for the brief consideration of the reaction of different types of tumors to irradiation, it was thought best to group the tumors into systems. In certain instances this was not possible; as, for example, in considering the tumors of connective tissue origin. Myoma and myosarcoma of the uterus are also tumors of the female genital system and in reality should be considered in that group rather than in the general group of connective tissue neoplasms. Therefore, an attempt was made to harmonize the groupings as nearly as possible, considering in the connective tissue class those tumors of connective tissue origin which could scarcely be discussed regionally. In constructing this outline, I have drawn entirely from the findings of the Memorial Hospital as recorded by Stewart. Considerable difference of opinion exists in regard to the relative sensitivity of certain tumors and in some instances these ideas differ sharply from those arrived at by Stewart. My reasons for accepting Stewart's opinions are based on the fact that they are more comprehensive than any others that I have been able to find. This is due to some extent to his enormous material, careful and unprejudiced follow-up, long observation of cases, and the fact that he presents only the actual results of irradiation without unnecessary argument or speculation.

NAME	RADIO-SENSITIVITY	COMMENT
	SKIN	
1. Basal cell epithelioma	Sensitive; resistance increases with adenocystic structure.	Very resistant when invading cartilage or bone.
2. Melanotic tumors	Very resistant.	In rare cases secondary skin implants may be sensitive.
3. Squamous cell epithelioma	Will be discussed under similar tumors of lip and mouth, where their reaction to irradiation is similar.	
4. For nevi, angiomas, etc., see tumors of lymphatic apparatus, and blood vessels.		
	GASTROINTESTINAL TRACT	
1. Adult squamous cell epithelioma of lip, dorsum, tip and lateral borders of tongue, alveolar ridges, hard palate, buccal mucosa, pharyngeal vault, true vocal cords.	As a group, resistant. The spindle cell epidermoid carcinoma in these same locations is highly resistant.	Gross characteristics very important. Papillary type more sensitive. Tumors of long duration more resistant because of tendency to fibrosis.
2. Papillary carcinoma of the anterior floor of the mouth.	Relatively sensitive.	Grossly vascular fungating growth. Histologically somewhat anaplastic and poor pearl formers.
3. Epidermoid carcinoma of tonsil, base of tongue and soft palate.	Moderately to highly sensitive. Even spindle cell carcinomas are sensitive when located posterior to anterior palatoglossal fold. Rare glandular types are resistant.	There are three main cell types as follows: (1) varying degrees of adult squamous cell carcinoma; (2) transitional cell carcinoma; (3) lymphoepithelioma, which are sensitive in the same order.
4. Metastases of squamous cell carcinoma to lymph nodes.	May be either more or less sensitive than primary growth; usually slightly more resistant.	Fibrosis and liquefaction increase resistance. Also, when capsule is penetrated and surrounding tissue is invaded, they are resistant. Normal nodes much more resistant than those containing carcinoma.
5. Parotid and submaxillary tumors, and adamantinoma.	Moderately resistant. Adamantinoma highly resistant.	Mixed tumors more sensitive than adenocarcinomas. Submaxillary carcinomas are usually resistant and aggressive.
6. Esophageal carcinoma.	Resistant. Anaplastic tumors show less regression than well differentiated types.	Anemia, emaciation, perforation and fibrosis increase the resistance.
7. Gastric carcinoma.	Sensitive cases very rare.	At Memorial Hospital a few have shown palliative response.
8. Carcinoma of the colon.	Resistant.	A few of the large fungating cellular carcinomas are sensitive.
9. Rectum		
a. Carcinoma.	Majority resistant. Colloid and stenosing types very resistant.	Cellular infiltrating carcinomas regress but recur promptly.
b. Epidermoid carcinoma.	Response similar to these tumors elsewhere.	
c. Lymphatic tumors.	Sensitive.	
d. Melanotic tumors.	Very resistant.	
	URINARY SYSTEM	
1. Kidney		
a. Carcinoma and hypernephroma.	Resistant.	Anaplastic metastases may be sensitive.
b. Epidermoid carcinoma of the kidney pelvis.	Uninfluenced by external radiation.	
c. Wilm's tumor.	Usually extraordinarily sensitive.	Recurrence is the rule.
2. Carcinoma of the bladder.	No accurate data.	Resistant to external radiation.

NAME	RADIO-SENSITIVITY	COMMENT
MALE GENITALIA		
1. Prostatic carcinoma	Resistant.	No results except with interstitial radiation. Takes 7 to 12 skin erythema doses for any results.
a. Bone metastasis.	Resistant.	Poor results from irradiation.
2. Testicle		
a. Adenocarcinoma malignum.	Moderately sensitive.	Hopeless after metastasis.
b. Embryonal carcinoma with lymphoid stroma.	Very sensitive.	Both primary growth and metastases can be sterilized.
c. Adult teratoma.	Resistant.	
d. Choriocarcinoma.	Relatively resistant.	Hopeless after metastasis.
FEMALE GENITALIA		
1. Ovary		
a. Embryonal carcinoma.	Quite sensitive.	Striking regression and massive resistant recurrence.
b. Granulosa cell carcinoma.	Sensitive if malignant.	Usually benign. If malignant, regression is usually followed by prompt recurrence and death.
c. Papillary cystomas.	Resistant.	Lower grades with implantations yield best results to radiation.
2. Uterus		
a. Corpus carcinoma (Healey & Cutler)		
(1) Papillary malignant adenoma.	Resistant.	Growth superficial, entirely papillary. Some cured with simple curettage.
(2) Uterine glands long and papillary, stroma scanty.	Resistant.	Cure of groups 1, 2 and 3 depends more on accessibility to huge doses of radiation.
(3) Adenocarcinoma.	Resistant.	
(4) Diffuse solid anaplastic carcinoma.	Sensitive.	Very anaplastic. Prognosis bad.
(5) Adenoacanthoma.	Resistant.	
b. Chorioepithelioma.	Probably sensitive.	Too few cases reported to know.
c. Myoma.	Regression.	Response probably due to action on ovaries.
d. Myosarcoma.	Some cases regress.	Probably none are cured.
3. Carcinoma of cervix		
a. Fully adult and somewhat undifferentiated types.	Relatively resistant.	No relationship between sensitivity and cure with present methods of treatment where all tumors receive about the same dosage.
b. Diffuse transitional forms.	Sensitive.	
4. Carcinoma of vulva and vagina.	Probably somewhat similar to carcinoma of the cervix since their structure is similar.	
5. Carcinoma of the breast.		
a. Intraductal adenocarcinoma or bulky adenoma malignum.	Sensitive. When capsule is penetrated they are resistant.	Irradiation accentuates tendency to spontaneous infarction. Irradiation effect not on tumor cell but blood supply.
a. Less cellular intracystic adenocarcinomas.	Sensitive.	Irradiation causes atrophy and calcification.
b. Comedocarcinoma.	Moderately sensitive.	Undergo calcification and necrosis. When cells penetrate the capsule they are resistant.
c. Diffuse duct carcinoma, so-called "inflammatory carcinoma."	Usually sensitive but incurable.	When a mass becomes palpable, they are less sensitive.
d. Small cell, highly malignant, duct carcinoma.	Very sensitive.	Metastasize widely and rapidly.
e. All other types of breast carcinoma are resistant.		
f. Axillary extensions.	Often obtain excellent regression with irradiation.	At Memorial Hospital, 5 portals are radiated with 550 roentgens each.
g. Skin metastasis.	No relation to resistance of primary.	
h. Lung metastasis.	Resistant.	
i. Bone metastasis.	Often good palliative results with irradiation.	Pain may be greatly reduced. Fractures may unite.
GLANDS OF INTERNAL SECRETION		
1. Thyroid gland		
a. Small cell carcinoma.	Resistant. Insufficient data with regulated dosage.	In some cases metastases in lung and bone have regressed following radiation of primary growth.
b. Large spindle and giant cell carcinoma.	Resistant.	
c. Papillary cystadenocarcinoma.	Some are moderately sensitive.	Some are probably not malignant.
d. Small round cell carcinoma—difficult to classify.	Resistant.	Have structure like a lymphosarcoma but do not involve glands.
2. Adrenal gland.		
a. Medullary carcinoma.	Unknown.	Usually widely metastasizing forms.
b. Small cell neurocytoma.	Very sensitive.	
3. Thymus gland		
a. Carcinoma.	Resistant.	
b. Group including lymphosarcoma, Hodgkin's, Sternberg type of hyperplastic tuberculosis, and endothelioma.	Sensitive.	Most of these tumors recur.

NAME	RADIO-SENSITIVITY	COMMENT
4. Pituitary gland		
a. Adenomas of anterior lobe with pressure on intermediate and posterior lobe.	Good results from irradiation.	
b. Tumors of third ventricle and midbrain, and supracellar cysts show no response.		
ORBITAL AND BULBAR TUMORS		
1. Melanomas and neurosarcomas.	Very resistant	
2. Lymphomas.	Sensitive.	Some resistant.
3. Liposarcomas.	Moderately sensitive.	Recur.
4. Neuroepithelioma and retinal blastoma.	Regress.	Recur.
5. Retinal glioma.	Regress.	May cure very small tumors.
TUMORS OF CONNECTIVE TISSUE CLASS		
1. Liposarcoma (fat tissue)	Marked or moderately sensitive.	Some tumors of this general group are cellular, very sensitive but may rapidly metastasize.
2. "Fascial" sarcoma.	Highly resistant with some exceptions.	The origin of many of these tumors is uncertain. They may be neurogenic, lipogenic, periosteal or pure myxoid types.
3. Skeletal muscle		
a. Rhabadomyosarcoma.	Resistant.	Rare tumors—only a few cases at Memorial Hospital.
4. Joints		
a. Complex group ranging from liposarcoma through xanthosarcoma to endothelioma and perithelioma.	As a group, resistant.	Histologically, they may appear sensitive but irradiation treatment is unsatisfactory.
5. Bone		
a. Benign giant cell tumor.	Great majority quite sensitive. Large tumors of tibia and femur in older patients and those penetrating the capsule respond poorly.	With secondary infection or recurrence following curettage, resistance increases. Some cases malignant at onset; some become so after recurrence.
b. Osteogenic sarcoma.	Resistant with rare exceptions.	The highly vascular cellular types may regress under radiation but recur.
c. Endothelial myeloma. (Ewing's tumor)	Very sensitive.	Most cases recur. A few cases resistant.
d. Other types of myeloma.	Highly sensitive.	
e. Xanthomatous tumors. (Christian's syndrome)	Sensitive.	Membranous bone defects heal.
f. Liposarcomas.	Sensitive.	
g. Metastatic tumors.	Will be considered under primary tumors.	
6. Nerve		
a. Neurogenic sarcoma.	As a group, resistant.	Adrenal and retroperitoneal neuroblastomas are quite sensitive.
b. Glioma (brain).	As a group, resistant.	Best results in astrocytomas and medulloblastomas. Few cases of spongioblastoma multiforme have shown complete regression of symptoms.
7. Blood vessels		
a. Spidery angiectases (Stewart)	Highly sensitive.	Yield to small amounts of Beta radiation.
b. Port wine nevi.	Moderate resistance.	Respond well in the young; resistance increases with advancing age.
c. Hypertrophic hemangiemas.	Moderate resistance.	
d. Angioendothelioma (Kaposi)	Resistant.	Angiome neuromyoarteriel (Masson) is highly resistant.
8. Lymphatic apparatus		
a. Lymphangioma.	Highly resistant.	
b. Lymph nodes, spleen and bone marrow.		
(1) Lymphosarcoma (lymphoid reticulocyte types)	Highly sensitive.	A rare case unaccountably resistant.
(2) Lymphadenoma (Brill Symmers), and lymphatic and myelogenous leukemia.	Very sensitive.	
(3) Hyperplastic and pseudoleukemic nodes.	Somewhat resistant.	
(4) Leukemic type Mickulicz disease.	Sensitive.	
(5) Hodgkin's granuloma.	Sensitive.	Sclerosing types may be resistant.

COMMENT

It is impossible in such a brief discussion to do more than touch upon the field of radiosensitivity. The only possible interest such a paper as this can have is to stress the fact that there is considerable accurate and valuable information on the subject, and that the best knowledge obtainable has been so admirably presented by Stewart that anyone more than passively interested in the reaction of tumors to irradiation should avail himself of Stewart's monograph and study it with great care.

CONCLUSIONS

The radiosensitivity of tumors is dis-

cussed and several of the factors which determine this reaction are enumerated with particular emphasis as to the necessity of thorough study of each separate neoplasm from many angles before rendering an opinion as to its response to irradiation. An outline is given which summarizes very briefly the reaction of most of the well known tumors to irradiation and very brief comments are given in many of these cases in an attempt to emphasize some of the important facts regarding their reaction to irradiation.

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THE MANAGEMENT OF EMPYEMA THORACIS

SAM H. SNIDER, M.D.*

At the outset we wish to point out that this discussion is not meant to cover chronic non-tuberculous empyema. The treatment of chronic non-tuberculous empyema is almost entirely a surgical affair and the management is a problem in surgery.

Empyema commonly occurs as a complication or sequel of lobar pneumonia or bronchopneumonia. Less frequently it occurs as a complication of spontaneous pneumothorax, and an occasional case is reported as due to fusospirochaetal infection without pneumonia. The latter type of case is extremely rare.

DIFFERENTIAL DIAGNOSIS

Before entering into a discussion of treatment it is well to emphasize the importance of making sure of the nature of the empyema that is being treated. A careful study of the history will usually show whether or not the empyema is due to an acute pneumonia or trauma. If it is not due to acute pneumonia or trauma, careful bacteriological study may be necessary to determine whether or not it is a tuberculous empyema. Empyemata complicating spontaneous pneumothorax may be due to either tuberculous infection or to acute pyogenic infection.

A chest should never be subjected to open drainage without first being explored with the needle and study of the pus made both grossly and microscopically. Stained smears will sometimes show tubercle bacilli even in the presence of acute pyogenic infection, and these cases should not be drained if drainage can be avoided.

PNEUMOCOCCUS AND STREPTOCOCCUS EMPYEMA

The ordinary empyema complicating pneumonia is usually found to be due to pneumococcus or streptococous infection and it is this particular type of empyema which we wish to discuss first. The first impulse on making the diagnosis of pus anywhere in the body is to institute open drainage for it appears that the pus should be immediately evacuated.

EARLY DRAINAGE

Let us consider for a moment the effects of early drainage in acute pyogenic empyema. The patient at this time is usually quite ill with pneumonia. The heart is embarrassed by the toxic state; the pulse is rapid and often weak. If the underlying pneumonia is of the secondary or bronchopneumonic type the other lung will usually show considerable involvement and in any case the pulmonary involvement acts for a considerable decrease of vital capacity. Let us suppose that drainage is instituted at this early stage of the disease. Adhesions have not formed in the pleural space and if open drainage be made the result is a large and extensive pneumothorax, which further reduces the vital capacity—often to an alarming degree. Furthermore, the infection is thereby rendered a universal infection of the pleural space and the draining sinus, even if properly located, is very remote from a large portion of the draining area. Hence, perfect drainage is difficult in such cases and with the extensive pneumothorax and lack of adhesions to act as a basis for closure, ultimate closure becomes difficult and often utterly impossible.

The arguments against early drainage may be summarized as: (1) Marked toxemia; (2) reduction of vital capacity by pneumonia; (3) further reduction of vital capacity by a large pneumothorax,

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and (4) difficult closure because of the large pneumothorax.

What should be done with the early empyema? The answer lies in aspiration by means of syringe or—even better—a Potain aspirator. By aspiration of the pus the vital capacity can be increased so that the patient can breathe more easily. Furthermore, if the pus is withdrawn to a low level the amount of pleural membrane bathed in pus is lessened and the amount of absorption from the pleural membrane is thereby decreased. Again—if the pus be withdrawn to a low level and kept to a low level, adhesions wall off the pus with the formation of a smaller pocket and make drainage at a later date more feasible.

LATE DRAINAGE

Let us consider the advantages of late drainage. If drainage is delayed until the toxemia of the pneumonia has subsided the patient is not nearly so ill, the heart has recovered from the toxemia to a certain extent, the pulse is less rapid and the patient in a generally better condition for operation. Furthermore, the clearing of the lung has resulted in a definite increase of vital capacity so that the patient has much less difficulty in breathing. Again—the keeping of the pus at a low level by aspiration will have resulted in formation of adhesions at a low level with only a small pocket for drainage. The drainage of this small pocket does not result in a wide-spread pneumothorax with its attendant disadvantages, but gives only a small pneumothorax which does not embarrass the patient's respiration so much, does not spread the infection extensively in the pleural cavity and leads to much earlier closure of the sinus because the area to be drained is rather closely adjacent to the draining sinus.

The advantages of late drainage may be summarized as follows: (1) Toxemia has largely disappeared; (2) vital capacity has already improved through clearing of pneumonia, and (3) through early aspiration a small pocket remains which leads to only a small pneumothorax and to earlier closure of the wound.

It should be further emphasized that the drainage should be made through an opening of sufficient size to permit insertion of a large caliber tube and that the site of the incision should be over the lowest draining point of the empyema when the patient is in either erect or dorsal position. This usually necessitates drainage near the base in the posterior axillary line but occasionally an empyema is encapsulated between the lobes of the lung and in this case careful study of physical findings and roentgen rays is necessary to locate the best site for drainage.

Our experience with dilute formalin solution in the handling of empyema has been limited and altogether disappointing. The pain attending the injection of formalin has been so marked we have not had the courage to continue its use. Likewise, our experience with gentian violet has been limited, not because of any alarming reactions, but because of disappointing results.

The Mazingo method of closed drainage is a very appealing method but one that involves considerable apparatus and rather definite mechanical difficulties. Our experience with it has been limited, and, while we believe it to be useful in a great many cases, our inclination is to adhere to the old dictum of early aspiration and late drainage.

TUBERCULOUS EMPYEMA

The onset of tuberculous empyema is often very acute as a result of the rupture of a cavity into the pleural space in a case that is being treated with artificial pneumothorax. The symptoms in such a case are usually severe pain in the chest, high fever, marked prostration and utter loss of appetite. In other cases of pneumothorax a pleural effusion may be the forerunner of a tuberculous empyema and the conversion of a serous effusion into pus may be very gradual. In these cases the symptoms may be very mild or the patient may be even practically symptom free. In any case of empyema which is suspected of being tuberculous, drainage should be approached with great caution because, owing to the chronic nature of the tuberculous infec-

tion, drainage persists for a long time and closure is very difficult to obtain.

The toxemia of these tuberculous empyemas may be relieved to some extent by aspiration. Aspiration may result in needle-track infections with resulting discharging sinuses, but even these sinuses can be closed by careful management, compression of the chest wall, without open drainage. It is the practice of the Matson Brothers and Bisaillon to aspirate tuberculous empyemas completely, thoroughly cleanse the cavity with saline solution and inject five per cent oil of gomenol in liquid petrolatum. I have varied this practice somewhat by injecting from one to three cubic centimeters of pure oil of gomenol directly into some remnant of pus left in the chest at the end of aspiration. This may result in severe reaction with pain, chill and fever, but no alarming symptoms have resulted in any of the half-dozen cases so treated. Some of these have promptly become symptom free and the pus has become sterile and gradually changed from thick to thin pus and then to serum again. Two cases of six so treated have become completely dry and we consider this to be a cure of the empyema. Other cases have required further aspiration but at prolonged intervals and the fluid has been thin pus or serous fluid.

Altogether, we consider the oil of gomenol treatment of tuberculous empyema to be a very great advance in the handling of this difficult condition.

SUMMARY

1. Differential diagnosis between tuberculous empyema and acute infectious empyema is necessary for intelligent treatment.

2. Acute pyogenic empyema is usually best managed by early and fairly complete aspiration with late open drainage.

3. Tuberculous empyema should seldom be drained.

4. Oil of gomenol has very great value in the treatment of tuberculous empyema.

UNIVERSITY OF KANSAS MEDICAL SCHOOL CLINIC

Idiopathic Hypochromic Anemia (Idiopathic Microcytic Anemia)

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The purpose of this paper is to call attention to a type of anemia which has been recognized as a clinical entity since the description by Kaznelson and Weiner in 1929[6]. This type of anemia was called cryptogenic Achylische Chloranamie by these authors, because of the absence of free hydrochloric acid in the gastric juices of their three cases. Since the original description numerous papers have been published under the following terms: Chronic Idiopathic Hypochromic Anemia, Primary Hypochromic Anemia, Erythro-normoblastic Anemia, Simple Achlorhydric Anemia, Essentielle Hypochrome Anämie, and Idiopathic Hypochromemia. The reason for our choice of Idiopathic Hypochromic Anemia is that this term was adopted by the National Conference Nomenclature of Disease in 1933, and in the University of Kansas Hospitals we are using this Standard Classified Nomenclature of Disease instead of the Bellevue Nomenclature which was used previous to this year.

Hypochromic anemia in adults is generally considered secondary to some other disease process, such as malignancy, infection, nephritis or hemorrhage. In fact, in the ordinary nomenclature (Bellevue) there is no recognition of the diagnosis of primary hypochromic anemia. This condition is obviously not chlorosis. The age distribution is entirely different, and furthermore chlorosis is frequently associated with hyperacidity in contrast to the anacidity found in this type of anemia. It is superfluous to add that before this diagnosis can be made, it is necessary to rule out other diseases which produce secondary anemia, especially gross or occult bleeding via the gastro-intestinal or genito-urinary tracts.

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All the writers agree the great majority of cases occur in females, and the fourth decade of life is the most common age group. Brown hair and eyes, said to be uncommon in patients with pernicious anemia, are fully as common in this type of anemia as blue eyes and brown hair. Although this disease picture was not recognized prior to 1929, cases are described in the literature which seem to belong here. In 1903 Einhorn[4] in his discussion of the possible relationship of achylia gastrica to pernicious anemia describes what appears to be a typical case of primary hypochromic anemia; the red blood count was 3,680,000 hemoglobin 30 per cent, leukocytes, 10,200 and a normal differential count. He concluded, "Although the blood picture in this case was not typical of pernicious anemia he was unable to interpret the disease other than pernicious anemia." At that time achylia was not recognized as a factor in pernicious anemia; in fact this author made the hypothesis that the achylia might result from atrophic changes in the gastric mucosa after the anemia had been present for a long time, analogous to the changes in the spinal cord.

The symptoms are those of any anemia, the characteristic features being the chronicity, the tendency to remissions and the relapses brought on by mild infections or increased exertion. The gastro-intestinal symptoms are probably the earlier and most constant ones, namely: Belching, anorexia, colicky pain and diarrhea. The latter is very often severe, persistent, and quite annoying to the patient. The other symptoms are: Dyspnea on exertion, weakness and fatigue, loss of weight, and less frequently sore tongue, paraesthesias and menorrhagia. In fact, Dr. Russell Haden[5] lists menorrhagia as a common symptom in achlorhydric anemia occurring in 10 of his 32 cases reported.

The signs obtained on physical examination are: Pallor, often quite marked, never associated with icteric tint as seen in pernicious anemia. The skin is quite often atrophic and inelastic. Occasionally changes in the tongue in the nature of Hunterian glossitis are found. Witts calls our attention to peculiar alterations in the nails of the hands and feet of a few of his cases[11]. These had typical hollow nails (koilonychia or spoon nails), so that a drop of water does not roll off when placed on the nail. The nails are also very tender and brittle. These changes disappear under treatment. Typical koilonychia have not been observed among our patients. Dameshek reports that the spleen is sometimes palpable[2], but splenic enlargement was not found in our cases.

Laboratory data: Gastric analysis shows complete absence or very low free HCl. Icteric index is usually lower than normal—blood serum rather pale. Blood findings: The hemoglobin is reduced more proportionately than the red count; that is, hypochromia of the red blood cells. Poly-chromatophilia and increase in reticulocytes are not ordinarily seen. The nuclei of the polymorphonuclear cells are usually many lobed, resembling the "pernicious anemia neutrophil." The lymphocytes are increased in relative number. Blood platelets are usually diminished during relapses and increased during remissions. Reticulocytosis during remissions may be as high as 10 per cent. Bone marrow biopsy: These findings were also described first by Kaznelson, Reimann and Weiner[6], biopsies being obtained from the sternum; despite the severe anemia, the leukopenia and thrombopenia—all of which would make one suspect some degree of aplasia of the bone marrow—the bone marrow was crowded with nucleated red blood cells. In contrast to the large number of megaloblasts seen in the hyperplastic bone marrow of pernicious anemia, all the nucleated red cells found in their cases were normoblasts. Normoblasts were found as high as 30 to 47 per cent in contrast to the normal 20 per cent. Biopsy after iron therapy showed the normal number of erythroblasts.

Treatment: One of the most characteristic features of the disease is the rapid and dramatic response to large doses of iron. The preparation of iron is left to the choice of the physician, the most favored being reduced iron and green iron

ammonium citrate, either with or without copper. The most important factor is the dosage, the optimum dosage being from three to six grams of iron daily during a relapse of the disease. During remissions the iron should be continued as the liver therapy is continued in pernicious anemia. Kaznelson in his original article noted that iron does not produce a permanent cure, but only remissions as long as it is continued. It is the usual practice to administer dilute hydrochloric acid in addition to the iron, although it is generally agreed that the blood response is just as rapid without.

CASE REPORTS

Case No. 1—M. D., married woman, 44 years of age, first presented herself in the medical dispensary of Kansas University on June 19, 1933, with the chief complaints of gas on stomach, nervousness, shortness of breath on exertion, persistent diarrhea, and indigestion. These symptoms had not been continuous but had recurred at irregular intervals, until the last several months when they persisted all the time. Of the above symptoms, the gastrointestinal were the more distressing to her; the feeling of upper abdominal distress and belching of gas, together with the diarrhea made her feel that she must have something very serious wrong with her. There was nothing striking about her stools except that she noticed mucus occasionally; never had blood been noticed in her stools. She also stated that her menstrual periods were becoming more frequent—every 21 days—and that the flow was more profuse. The patient had been seen previously in the gynecological clinic where negative pelvic findings were reported. There was nothing significant in the history of past illnesses or family history of this patient.

Physical Examination: Slender, moderately well nourished, white female, 44 years of age, with an obvious pallor of the skin, sclera and other mucous membranes, did not appear acutely ill but was short of breath on exertion. Tonsils slightly enlarged, no adenopathy. Lungs and heart were negative. Blood pressure 106/60. The abdomen was flat; there was vague tenderness over the upper abdomen, but no rigidity, palpable organs or masses.

Laboratory and x-Ray Findings: Urine examination repeatedly negative. Red blood count 4,340,000, and hemoglobin 37 per cent. Because of the marked discrepancy between the number of red blood cells and hemoglobin, the count was repeated a few days later and the red blood count was 4,600,000 and hemoglobin 37 per cent. The white count was 8,600 with a normal differential count. Gastric analysis showed no free HCl in any of the four specimens taken at hourly intervals, and the highest total acidity was 5. Gastro-intestinal series and chest plate were negative for pathology, except for increased irritability of the colon.

Progress and Treatment: The patient was given reduced iron gr. XXX daily and dilute HCl gtts. XXV, t.i.d. with meals, and one month later the blood count was R.B.C. 4,190,000, 68 per cent hemoglobin, W.B.C. 8,650, polymorphonuclears 69 per cent, lymphocytes 29 per cent, eosinophiles one per cent, and monos one per cent. The patient was feeling stronger and was less dyspneic, but was still complaining of gas on her stomach and diarrhea. For this reason she was sent into the hospital for a more complete examination, especially with reference to the diarrhea, and her increased menstrual flow. Nothing additional was found in the hospital. Stool examinations were negative for gross or occult blood. Gastric analysis again showed absence of free HCl.

Pelvic examination by the gynecological consultant negative. The patient was dismissed from the hospital about the middle of October, 1933, and has been followed in the dispensary. She has continued to take reduced iron gr. X, t.i.d and dilute hydrochloric acid drams one in tomato juice with her meals. One month after dismissal from the hospital and exactly two months after initiation of specific therapy the red blood count has risen to 5,120,000 and hemoglobin to 83 per cent; the white count and dif-

ferential remained normal. The diarrhea has subsided entirely, in fact, she now has to take laxatives occasionally. Her menorrhagia has also disappeared, the flow now being scanty and a few periods have been missed.

Subsequent blood counts:

December 14, 1933—Hgb 84 per cent; R.B.C. 5,050,000; W.B.C. 6,350.

January 29, 1934—Hgb 81 per cent; R.B.C. 4,220,000; normal differential.

March 19, 1934—Hgb 81 per cent; R.B.C. 4,160,000; W.B.C. 7,200.

Case No. 2—L. B., white female, 43 years of age, admitted September 19, 1933, complaining of anemia, shortness of breath, numbness of fingers and toes, and palpitation on exertion. She also complained of dizziness and gas on her stomach.

The physical examination was entirely negative except for the obvious pallor. Gastro-intestinal fluoroscopy negative for pathology and stool examinations were negative for blood or parasites.

Blood count on admission: 3,950,000, hemoglobin 45 per cent, color index .57, leukocytes 8,500 with 72 per cent polymorphonuclears.

The patient was given reduced iron gr. X, t.i.d. together with small amount of dilute hydrochloric acid and no other treatment. One month later the blood count had risen to 4,390,000, hemoglobin to 74 per cent, and color index to .84. The treatment was continued and two weeks later the red count was 4,830,000, hemoglobin 84 per cent and color index .87.

Case No. 3—F. B., white female, 30 years of age, came to the medical dispensary during the summer of 1933 complaining of gas, recurrent diarrhea, shortness of breath and weakness. The physical examination and *x*-ray studies were negative. The blood count was 4,120,000, hemoglobin 61 per cent, color index .7 and leukocytes 9,000, with a normal differential count. This patient was given Blauds pills III, t.i.d. together with dilute HCl gtts X, with meals, and four weeks later the blood examination showed: 5,130,000, hemoglobin 74 per cent, and four months later the blood count was 4,670,000 with 85 per cent hemoglobin. Her admission symptoms, epigastric distress, recurrent diarrhea, nervousness, and dyspnea had all disappeared, and she has continued in good health to the present time under iron medication.

DISCUSSION

The fact that this type of anemia is called primary or idiopathic is enough evidence that the etiological factor is unknown, but all agree that the achlorhydria is a predecessor of the anemia and a constant associated finding. Witts[11] and Mills[8] both point out that there may be a relation between this type of anemia and pernicious anemia. It would seem probable that these two types of anemia are manifestations of a common defect, and this defect is achlorhydria, either congenital or acquired. One point in favor of this fact is the frequent occurrence of anemia after total or partial gastrectomy; both macrocytic and microcytic types of anemia occur but the latter is more common. In the male achlorhydria more often is associated with or produces a megalocytic (macrocytic) anemia; in the famale a microcytic anemia. In both forms the bone marrow is hyperplastic, with the predominance of megaloblasts in pernicious anemia and of normoblasts in primary hypochromic anemia. Witts suggested that this inhibition to the normal maturation of the red cells in the bone marrow was due to the absence of a hormone produced in digestion by the healthy stomach.

Mettier, Kellogg, and Rhinehart proved that anemia in these patients was not due to iron poor diets. They reported 10 cases of primary hypochromic anemia in females. Three of their cases were put on iron diets very rich in organic iron, 16 to 20 mg., which is several times the normal amount of dietary iron. After 60 days on this diet, there was no material change in their red count or hemoglobin readings. Subsequently the same three patients were given six gm. of iron and ammonium citrate daily and they showed an average increase in hemoglobin of 30 per cent in one month. Kaznelson pointed out in his original paper that

iron was not only specific for this type of anemia, but also that it relieved the distressing symptoms of gastro-intestinal origin. He reported a case of a white female, 67, who consulted her physician because of severe diarrhea, belching, abdominal pain, and anorexia. These symptoms had been present off and on for 20 years, and there had been a 40 lb. weight loss during the year prior to admission. She was given reduced iron, gr. VIISS, t.i.d. All of her symptoms were relieved in a few days, and improvement continued as long as iron was administered.

Kaznelson, Reimann and Weiner also made studies of the flora of duodenal contents of their patients, both in remission and relapse, as has been done in many cases of pernicious anemia. They found a sterile or very small bacterial flora in contrast to the prolific flora in duodenal contents of pernicious anemia patients. The only organisms found were enterococcus and non-hemolytic coli; and never did they find hemolytic coli. For this reason they concluded gastro-intestinal flora has nothing to do with the anemia.

Because of the fact that we have not been recognizing this type of anemia until the past year, we have reviewed 100 cases in which the diagnosis of achlorhydria alone was made. All cases in which there was a possibility that the anemia could be secondary were excluded. The great majority of these cases had adequate *x*-ray examination to rule out ulcer or malignancy, and many showed negative tests for occult blood in the stools. No pernicious anemia cases were included.

It can be seen from the study of the data in Table 1 that women are more likely to develop anemia. There is very little difference as to sex under 30 years of age, but from then on there was a marked difference in the blood counts. Between the ages 30 to 40 the average hemoglobin in the men was 90.5 per cent and in the women 69.5 per cent; however, the difference in the red count was not so marked. Between the ages 40 to 50 the average hemoglobin in men was 83.4 per cent, and in women 70 per cent. Between the ages 50 to 60 the average hemoglobin in men was 84 per cent and in women 74 per cent, and above 60 years of age the average hemoglobin in men was 84.6 per cent and in women 72 per cent.

SUMMARY

1. Three typical cases of Idiopathic Hypochromic Anemia are described, with rapid improvement under iron treatment.

TABLE 1
Analysis of 100 Cases of Achlorhydria

Age Groups	Sex	Cases	Average R. B. C.	Average Hb %	Average Color index	Average Leukocytes
Under 30	Male	5	4,870,000	86	.89	6,950
	Female	5	4,510,000	80.5	.89	8,900
30-40	Male	13	4,870,000	90.5	.93	7,250
	Female	12	4,180,000	69.5	.83	8,150
40-50	Male	9	4,590,000	83.4	.91	8,050
	Female	14	4,690,000	70	.74	6,850
50-60	Male	8	4,890,000	84	.86	7,750.
	Female	14	4,265,000	74	.89	7,950
Above 60	Male	13	4,700,000	84.6	.90	7,100
	Female	7	4,850,000	72	.75	7,250

Analysis of 100 cases of achlorhydria, giving the blood counts with special reference to sex and age groups. Note: All of these cases were taken from the Bell Memorial Hospital records, and the primary diagnosis was achlorhydria—gastric analyses all showing complete absence of free hydrochloric acid after the fractional test meal. The majority had gastro-intestinal x-ray studies and stool examinations to rule out gross and occult blood loss, which might account for the anemia. Leukemias, pernicious anemia, menorrhagia, etc, are excluded from this series.

2. Idiopathic Hypochromic Anemia is a clinical entity as definite as pernicious anemia, and is a frequent source of illness in women between the ages of 30 to 50 years.

3. One hundred cases of achlorhydria are reviewed with special reference to the blood counts, comparing the sex and age groups.

4. If untreated, this disease is chronic, and may or may not show spontaneous remissions. The majority of writers believe that spontaneous remissions are not found.

5. The typical blood picture—microcytosis, hypochromia, low red blood count and low color and volume indices—together with the findings in the bone marrow both in relapse and remission, is described.

6. The symptoms—achlorhydria and response to iron therapy—indicate that the fundamental cause of the anemia is a deficiency in the absorption or utilization of iron.

7. That this type of anemia does not respond to liver therapy, speaks for the fact that it is entirely different from pernicious anemia and is further evidence for the specificity of liver treatment of pernicious anemia.

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CASE REPORTS

Non-Specific Prostatitis

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Chronic nonspecific prostatitis is one of the most trying maladies the physician is called upon to diagnose and treat. As it frequently happens, where little is known much is written; so in prostatitis, volumes have been written, most of which is chaff driven by the wind. A large percentage of patients afflicted with this disease are neurotic. Whether it is because of the disease or not is not always clear. Many of these chronic prostatitis cases are also sexual neurotics, and have temporarily lost their erectile power. To go into the historical background, the symptomatology and diagnosis in complete detail would cover more than my allotted time.

HISTORICAL

The various estimates from large numbers of patients studied range from 50 to 90 per cent that have had a gonococcus infection at some time prior to the onset to the chronic prostatitis. As this is about the average estimate of the incidence of gonococcus infection in males generally, I am one who believes that a gonococcus infection has nothing whatever to do with average non-specific prostatitis, even if the patient states that sometime, 10 or 20 years before, he had a gonococcus infection. However, I do believe that a history of other focal infections, such as infected teeth, tonsils, sinuses or hemorrhoids, have a marked influence on these conditions. I believe strongly that the practice of masturbation, so common among youth, is a factor in nonspecific prostatitis, to say nothing of the necking parties so frequently indulged in by our youth of today.

SYMPTOMATOLOGY

The symptoms are so numerous and varied that they may be considered as arising from three main causes: (1) By infection blood borne from foci to the

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prostate; (2) by toxins blood borne from foci in the prostate gland, and (3) by reflex nervous impulses originating in the prostate gland and resulting in pain at distant points as neurotic symptoms.

I shall present a case illustrating each of the above divisions. A man, 46 years of age, was sent by an ophthalmologist for a prostatic check-up to see if there might possibly be some connection between the eye condition and a possible prostatic infection. The man had an iritis of unexplained origin. His Wassermann was negative. He had never had a gonococcus infection. He had no symptoms referable to his prostate. He had no demonstrable focal infection in his teeth, tonsils, sinuses or hemorrhoids. Examination of his prostate revealed a moderate amount of pus in the expressed secretion, together with pus casts and strings of pus. The striking feature was that the iritis was made distinctly worse by the manipulation of the prostate incident to the examination. We waited until the eye condition quieted down before attempting further prostatic treatment. This illustrates a prostatic infection which gave the patient no symptoms other than an eye infection, but the prostate was acting as a distinct focus of infection. I believe that this is a quite uncommon occurrence, but it does happen often enough so that one must be careful not to overlook the condition in such cases.

The second group may be represented by the next case, which is a man, of the educator type, 39 years of age, married, who has been suffering from attacks of angioneurotic edema for a long time. He was sent to me by an internist who desired a careful check of his prostate (I think it is of more than passing interest to note that five years before, I removed a very large hyperplastic type of prostate from this man's father). The patient had not had any edematous attacks for sometime prior to the time of my examination. He was apparently in a quiescent stage. I made the usual examination and found the prostate very large and boggy and the secretion expressed was almost purulent. Within an hour of the time of that manipulation of the gland he had an attack of edema and his lip swelled to enormous size and he became quite ill. It required a six months course of treatment to cure this patient. He has been well for over 18 months.

Another case which will illustrate the third group, is that of a married man, 47 years of age, who became enamored of his secretary, and who then found he had lost his virility. Numerous unsuccessful attempts at sexual relations caused so much congestion of his prostate that a severe nonspecific prostatitis ensued. He came for the relief of the loss of erectile power. Of course, like most cases of "lost manhood," not due to advancing years, this was a mental state. In dealing with such cases one sometimes needs the aid of a trained neurologist.

There are many other types of this disease beside the three mentioned, but in general these will serve as examples. That chronic nonspecific prostatitis is a forerunner of prostatic enlargement in later years, there can be no doubt. That nonspecific prostatitis has any connection with previous gonococcus infection, I believe, has never been proven.

A word as to treatment: (1) First, and most important, is a complete physical examination with special reference to focal infections, including hemorrhoids and their eradication. (2) The use of some foreign protein intramuscularly. (3) The urethra must be examined with a urethroscope for stricture and dilatation with the Kollman dilator instituted. (4) Prostatic massage never more often than twice a week and once a week is better. (5) Heat locally, in fairly severe cases, hot sitz baths twice a day are of value. (6) Tonics containing appropriate vitamins to build up general health.

Whenever one gets to the place where the progress of a cure seems halted, one must stop all treatment and ask the patient to return in six weeks. Sometimes the result is surprising, since the patient goes on and gets well when left alone. Prostatitis cases in general are very trying because the average busy practitioner gets tired of trying to take care of a patient who frequently is non-coopera-

tive and unappreciative of the effort being put forth to cure him. He thinks he ought to get well in some miraculous manner and as a rule he is never treated for sufficiently long time to get well.

The Mechanisms of Polyuria in Diabetes Mellitus and Diabetes Insipidus

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It is an interesting fact that the polyurias of diabetes mellitus and diabetes insipidus are due to entirely different mechanisms. The two diseases have the common basic name, "diabetes," indicating the excretion of an excessive quantity of urine. Beyond that point, with the exception of thirst, there is no resemblance between the two diseases. The available textbooks of medicine contain nothing explanatory of the polyuria of either disease. The urine in diabetes insipidus is of low specific gravity, contains no sugar, and there is no elevation of blood sugar. In fact, the blood sugar in this disease may be lower than normal. In untreated diabetes mellitus the specific gravity of the urine is increased, it contains sugar, and the glucose in the blood is always above the normal level.

We wish to present an illustrative case of each disease as observed in children of approximately the same age, and to follow with a brief discussion of the theories relative to the polyuria seen in these cases.

Diabetes Insipidus: Case A. Z. (Hospital No. 48740) is a white school girl, age 12. She was first admitted to the hospital in August of 1932, with the chief complaint of polyuria and polydipsia. The onset of this trouble was in 1931 when the patient was nine years old. It was not known whether it began gradually or abruptly. She suffered from great thirst, polyuria and loss of weight, which were progressive until the time of her entrance into the hospital one year later. She drank large quantities of water frequently. There was a diurnal and nocturnal polyuria. Enforced restriction of water decreased the daily output of urine to an undetermined extent, but made the patient suffer extreme thirst, with dry mouth and lips. At the time of her first admission she was getting up as many as ten times between 8:00 p. m. and 6:00 a. m. to pass her urine. She recently has been admitted to the hospital a second time (March, 1934). Since her previous admission nearly two years ago she has taken one-half ampoule of pituitrin intranasally morning and night. There has been complete relief of symptoms. She has gained 14 pounds and has grown three and one-half inches taller. She is now 56½ inches tall and weighs 71 pounds, which is the normal average for girls of her age.

The personal and family history, as well as the physical examination, are entirely negative.

The laboratory findings after administration of pituitrin are as follows: The urine acid in reaction, specific gravity 1.012, and negative for sugar and albumen. Blood count and hemoglobin normal. Nonprotein nitrogen is 28.5, creatinine 1.3, and sugar 87. Wassermann and Kahn are negative. Glucose tolerance and renal function tests are normal. *x*-Ray of the skull shows no abnormality. Ossification centers in the wrists are consistent with the age of the patient. The basal metabolic rate is plus 41, a fact frequently observed in this disease, but as yet unexplained.

When taking no pituitrin the daily fluid intake is 8,000 cc. (266 ounces) and the urine output 11,000 cc. (366 ounces). The child voids 300 to 500 cc. (10 to 16 ounces) every one to two hours, and has to get up frequently during the night. When taking one-half ampoule of pituitrin intranasally morning and night she does not get up at night; the 24 hour urine output is 2,900 cc. (96 ounces) and the fluid intake is 3,400 cc. (113 ounces).

Diabetes Mellitus: Case D. H. (Hospital No. 48489) is a 13 year old white school girl admitted to the hospital with "sugar diabetes." She was diagnosed as

*Department of Pediatrics.

diabetes one year ago by her local physician. At that time she was suffering from polydipsia, polyuria, nocturia, and weakness, and also had an acetone odor upon her breath. Her blood sugar was found to be 192 mg. per 100 cc. and her urine sugar free. It was deemed advisable to put this patient on a high carbohydrate diet adequately covered with insulin, upon the assumption that this procedure would prevent further insult to the remaining normal pancreatic tissue. Therefore, she was fed 400 grams of carbohydrate, 120 grams of protein, and 120 grams of fat, daily, along with 45 units of insulin. Under this regime, however, the blood sugar was constantly over 200, and sugar was always present in the urine. The diet was reduced to 150 grams of carbohydrate, 25 grams of protein and 50 grams of fat, daily, with 35 units of insulin distributed as follows: 15 before breakfast, 15 before supper and 5 at 2:00 a. m. During her stay in the hospital she was taught to compute her diet, to properly administer insulin, and to analyze her urine for sugar. She was dismissed after a two weeks' stay with the blood sugar within normal limits and the urine sugar free.

The following table gives the summary of laboratory findings and fluid status, recorded at an eight-day interval:

TABLE 1

	March 2, 1934	March 10, 1934
Sugar in mg. per 100 cc. of blood.....	227	172
Total water intake in 24 hours	3,100 cc.	1,425 cc.
Total 24 hour urine output	4,910 cc.	1,100 cc.
Total 12 hour urine output, 10 a.m.-10 p.m.	3,495 cc.	900 cc.
12 hour output of sugar in urine	20.9 gms.	none
	C P F	C P F
Diet	400-120-120	150-25-50 (50)
Insulin	U 10-10	U 20-20-5

Table 1 illustrates the fact that the daily quantity of urine decreases simultaneously with the reduction of sugar in the blood and urine through the effect of insulin.

DISCUSSION

The kidneys have many important functions in addition to urinary excretion. They maintain osmotic balance between the tissues and the blood, keep the constituents of the plasma at an optimal concentration, eliminate waste products, maintain blood volume and blood reaction constant within narrow limits, and eliminate acids and toxins. The mechanism involved in renal function is not yet fully understood. The theory[1] of urinary excretion generally accepted by physiologists is as follows: the glomeruli act as simple filters, allowing the passage of a fluid into the tubules which differs from the blood plasma only in its lack of proteins. This process is a physical one regulated by the glomerular pressure, rate of flow of blood through the kidneys, composition of the blood, and character of the glomerular epithelium. According to Cushny the glomerular filtrate is modified by a process of differential absorption as it passes through the tubules. Thus, sugar undergoes complete tubular resorption, while such substances as creatinine and sulphates are concentrated about 80 times. Water is re-absorbed as needed to maintain a constant blood volume. If the tubules simply absorbed water from the glomerular filtrate the concentration of substances in the bladder urine and plasma would be identical. Simply stated, the glomeruli act as filters barring only the passage of plasma proteins while the tubules sort out the constituents of this filtrate, re-absorbing some, and concentrating others to form the urine as we find it in the bladder, very different in composition from the plasma. We have found in children of 10 to 12 years of age that the average daily fluid intake is 1,800 cc. (60 ounces) with an average daily urine output of 2700 cc. (90 ounces). Both values normally vary over a wide range.

In diabetes insipidus there is an excessive excretion of dilute urine, with faulty absorption of water by the tubules, other blood constituents being normally absorbed. The direct cause of the polyuria, however, is more obscure and may

be attributed to one of several factors which were summarized by Fitz[2]. It is his idea that polyuria results from the failure in the function of the kidney to concentrate urine. He states that the cause of the polyuria may be primary in the kidney, and explain the polydipsia. A further explanation is the possibility that the polyuria is symptomatic, being induced by stimulation of the kidney from hypersecretion of the hypophysis.

Wright, however, takes the opposite view. He finds good evidence that the pituitrin acts by stimulating the epithelium of the convoluted tubules to increased absorption. He feels, therefore, that faulty absorption of water by the tubules is the mechanism of polyuria in diabetes insipidus. There is no evidence that pituitrin acts by altering the blood supply of the kidney. It does, however, cause an increased renal activity as the oxygen consumption of the kidney is notably increased following the administration of pituitrin.

It seems to us, however, that the two foregoing apparently differing opinions of Fitz and Wright are not inherently at variance because they both consider faulty absorption of the urine by the kidneys as the fundamental cause of the polyuria in diabetes insipidus.

Illievitz[3] found a substance of unknown chemical composition in the urine of patients with diabetes insipidus. This substance was not found in the urine of patients in whom polyuria was experimentally induced. He did not prove, however, that the substance with which he was working accounted for the polyuria.

Helen Bourquin[4] reported a diuretic substance present in the urine of dogs with experimental diabetes insipidus. She has prepared an extract of the mammillary bodies and thalamus of the normal brain which has a diuretic effect.

The polyuria of diabetes mellitus results directly from the hyperglycemia. The increased sugar in the blood increases the osmotic pressure of the blood and thereby dehydrates the tissues of the body. This results in an increase in blood volume with a relative increase in the water content of the blood. This in itself would increase the urine output somewhat. There enters into this diuresis a second factor, namely the physiological process of "tubule diuresis," a term used by Wright.

A tubule diuresis is caused by the presence in the blood and consequently in the glomerular filtrate of a non-threshold substance. An example of such a substance is sodium sulphate. Sodium sulphate when given intravenously is all excreted in the urine and there is no re-absorption of this substance by the tubules. The maintenance of proper dilution of the sodium sulphate so that the osmotic pressure of the tubule fluid will be within normal limits requires additional water in the tubule fluid. This means increased output of urine, or more concisely, diuresis.

All sugar in the blood *above the normal level* acts similarly as a non-threshold substance. The presence of the sugar in the tubule fluid, through its osmotic pressure, prevents the normal absorption of water by the tubules. With less water re-absorbed by the tubules there results an increase in urine output. According to this theory, the more sugar present as a non-threshold substance the greater should be the urine output. This proves to be the case as is seen in severe cases of diabetes mellitus with high blood sugar levels.

SUMMARY

1. A case of diabetes insipidus in a girl of 12, and one of diabetes mellitus in a girl of 13, are presented.

2. The mechanism of the polyuria in diabetes insipidus is thought to be a faulty re-absorption of water by the kidney tubules. Various theories of the cause of this abnormality are presented.

3. The mechanism of the polyuria in diabetes mellitus is a physical phenomenon caused by excessive amounts of non-threshold sugar in the glomerular filtrate. This sugar through its osmotic pressure causes an increased excretion of urine.

4. The symptoms in this case of diabetes insipidus were completely alleviated by intranasal pituitrin one-half ampoule twice daily. Education and co-operation of the child, a measured diet,

and adequate insulin satisfactorily controlled the symptoms in the case of diabetes mellitus.

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TUBERCULOSIS ABSTRACTS

Furnished through the courtesy of The Kansas Tuberculosis and Health Association

As early as 1884, Weichselbaum described the presence of acid-fast bacilli in the blood of tuberculous patients. Scores of workers have since identified tubercle bacilli in the blood of patients with various forms of tuberculosis. A few have reported the occurrence of tuberculous bacillemia in cases with no evidence of tuberculosis. Löwenstein particularly claims to find tubercle bacilli in the blood in many non-tuberculous clinical conditions. Pronouncements based on such reports have led to the hypothesis that many clinical conditions of doubtful etiology are of a tuberculous nature. What evidence is there to support this doctrine? Tuberculous bacillemia was studied by G. S. Wilson and his colaborators. Their report was published as a 150 page brochure by the Medical Research Council of Great Britain. High points of the report are here quoted.

Tuberculosis Bacillemia

Marked discrepancies occur in the results of workers who have endeavored to demonstrate the presence of tubercle bacilli in the blood by microscopical examination. Some have failed to find tubercle bacilli even in advanced cases of tuberculosis while others claim to have found them in every case of pulmonary and non-pulmonary tuberculosis examined as well as in a high proportion of patients suffering from non-tuberculous disease and of perfectly healthy persons.

The microscopical techniques employed show two main sources of error: (a) confusion caused by artifacts such as fibrin threads, partly disintegrated leukocyte granules, lipoid portions of the red cell envelope, etc., and (b) confusion caused by contamination of the preparations with saprophytic acid-fast bacilli, which are frequently present in tap and in old distilled water and in reagents made up with them.

A surprising degree of discrepancy is noted also in the results of different workers who have endeavored to demonstrate the presence of tubercle bacilli in the blood by the guinea pig inoculation method. These discrepancies are undoubtedly attributable to faulty diagnoses of the inoculated animals, based on insufficient grounds. However, the animal inoculation method as practiced by capable workers is probably the most reliable means of demonstrating the presence of virulent tubercle bacilli. Records of those workers, whose competency seems to be assured, revealed that only a small number of positive results have been obtained, most of which have been with blood from patients suffering from miliary tuberculosis, tuberculous meningitis, advanced pulmonary tuberculosis and occasionally surgical tuberculosis.

Löwenstein has worked out a technique of blood culture with which he has been able to obtain a surprisingly high proportion of positive results, not only in definite cases of tuberculosis but in a number of diseases, the tuberculous nature of which is not generally recognized. The investigators found it difficult to analyze and evaluate the work on which this claim is based. They point out numerous anomalies and contradictions in the results obtained by Löwenstein and subsequent workers who endeavored to duplicate his technique. One of the greatest difficulties encountered was the incomplete and confused nature of the records published by Löwenstein.

CONCLUSIONS

The investigators conclude without equivocation that tuberculous bacillemia, except in patients suffering from advanced and grave disease, is a rare and sporadic phenomenon.

"In diseases such as articular rheumatism, polyarthritis, chorea, multiple sclerosis, schizophrenia, retrobulbar neuritis, Hodgkin's disease, and certain af-

fections of the skin, which are not accompanied by gross lesions of tuberculosis, there is practically no evidence that a tuberculous bacillemia ever occurs, nor are there any sound reasons to suppose that the tubercle bacillus plays any essential role in their etiology."

Tuberculous Bacillemia, G. S. Wilson, Medical Research Council, London.

Progress in tuberculosis control and treatment is well reflected in the annual reports of sanatoria that come to hand. One such report is that of the Tuberculosis Service of Bellevue Hospital New York City for 1933 prepared by James Alexander Miller Physician in Charge. A few excerpts of particular interest follow.

Modern Tuberculosis Service

The Service is divided into four main groups: (1) The Wards, (2) Out-Patient Clinic, (3) Day Camp and (4) Settlement House. The four wards, with a total normal capacity of 174 have been overcrowded, the winter census running as high as 240. During 1933 there were discharged 2,280 cases of tuberculosis and 533 cases of non-tuberculous conditions. About 15 per cent of the patients are convalescent and ambulant, 35 per cent are chronic bed cases and 50 per cent are acute cases. The cases admitted include an average of 15 to 20 per cent of patients with chronic lung diseases who are found not to have tuberculosis. These are not discharged because of their non-tuberculous condition but receive special treatment.

Collapse therapy is changing the whole trend of the care of the tuberculous. Approximately 40 per cent of all cases of pulmonary tuberculosis are benefited by some form of collapse therapy. An average of 27 pneumothorax treatments per day are given. One hundred thoracoplasty operations were performed during the year.

OUT-PATIENT WORK

The Out-Patient Department admitted last year 2,063 cases. The rotation of physicians between the Ward and Out-Patient Department services makes cooperation between the two effective. An important new field of activity has been the pneumothorax clinic for ambulatory cases. During 1933, 3,329 pneumothorax treatments were given. This work has opened up a new field of medical effort for it enables many patients to stay at home while continuing their treatment and at least one-fourth of them are able to continue at work. This increasing class of cases is another striking evidence of the change of emphasis from one on health resort and sanatorium treatment to home and institutional treatment in centers of population.

A very important feature of the Out-Patient Department is the supervision of home conditions through the visiting nurses of the city and the bringing in of contacts for examination. The children's clinic is largely constituted of this class of cases. The provision of material relief by the proper agencies is not neglected.

The Day Camp for cases that do not need full sanatorium care is really a floating hospital moored in the river adjoining the hospital grounds. During the year the census of the day camp has averaged 30 men, 15 women, and 75 children. The maintenance expense is comparatively small but the results have been extraordinarily satisfactory.

Bellevue Settlement House, which has a capacity of about 22, renders a very useful service for girls with tuberculosis who are without suitable homes, either while waiting to go to, or after returning from, a sanatorium. The entire expense of the Settlement House is borne by private funds through the Women's Auxiliary.

SUPPLEMENTARY SERVICES

Collateral activities of the Bellevue Tuberculosis Service include (1) Education in chest diseases for undergraduate and postgraduate students. (2) Special training of the medical staff. (3) Social Service, including the activities of the Women's Auxiliary. (4) Cooperative efforts in the development of modern chest surgery. (5) Pathological and clinical laboratory work, including scientific research. (6) Contributions to medical literature.

The Service is chronically overcrowded and overworked. All patients who apply to the hospital must be admitted and since the total number of tuberculosis beds in New York City as a whole has been markedly diminished in the past ten years transfers to other institutions are often delayed. The popularity of the Service has made patients eager to be admitted and reluctant to be transferred. The depression has added heavily to the burden. Plans for expansion of the Service are not wanting and it is hoped that these will receive most careful consideration.

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THE PHYSICIAN'S LIBRARY

SURGICAL ANATOMY: By Grant Massie, M.B., M.S. (London), F.R.C.S. (Eng.) Assistant Surgeon, Guy's Hospital; Surgical Tutor, Guy's Hospital Medical School; Examiner in Anatomy for the Fellowship of the Royal College of Surgeons of England; Late Senior Demonstrator of Anatomy, Guy's Hospital Medical School. Second edition, enlarged and revised, published 1933. Octavo, 458 pages, with 147 illustrations, many in colors. Lea & Febiger, Philadelphia. Price $6.00.

An exceedingly useful book for the surgeon who desires to refresh his knowledge of anatomy quickly. The topics are clearly presented. The illustrations in the main are excellent and the field is well covered. —C.E.J.

THE TECHNIC OF LOCAL ANESTHESIA: By Arthur E. Hertzler, A.M., M.D., Ph.D., LL.D., F.A.C.S. Professor of Surgery in the University of Kansas; Surgeon to the Halstead Hospital, Halstead, Kansas; to St. Luke's Hospital and St. Mary's Hospital, Kansas City, Missouri, and to the Providence Hospital, Kansas City, Kansas. Fifth edition. 148 Illustrations. The C. V. Mosby Company, St. Louis. Price $5.00.

The book is written in Dr. Hertzler's characteristic style; the Fifth Edition is devoted almost entirely to infiltrative anesthesia. The illustrations are excellent. The technic is thoroughly described and the book should be useful for any one using this form of anesthesia. There are chapters on paravertebral and splanchnic and a chapter on spinal anesthesia. The subject matter is concisely and exceptionally well illustrated.—C.E.J.

HYPERTENSION AND NEPHRITIS, by Arthur M. Fishberg, M.D., Associate Physician to Beth Israel Hospital; Associate in Medicine, Mount Sinai Hospital, New York City; Third edition, thoroughly revised; Illustrated with 39 engravings and 1 colored plate; Lea & Febiger, Philadelphia, 1934; Price $6.50 net.

In this third edition we have a very comprehensive treatise on hypertension and nephritis. The work on nephritis alone is taken up in clear terms and very complete. The work on blood pressure takes up all the various theories of the cause of blood pressure and combined with the part of kidney damage shows the treatment and expectancy. This book would be very valuable to the general practitioner as well as the internal medicine man for reference.—C.K.S.

ALLERGY IN GENERAL PRACTICE, by Samuel M. Feinberg, M.D., F.A.C.P., Assistant Professor of Medicine and Attending Physician in Asthma and Hay Fever Clinic, Northwestern University Medical School; Professor of Medicine in the Cook County Graduate School of Medicine; Attending Physician Cook County Hospital, Chicago. 330 pages. Illustrated with 23 engravings and a colored plate. Lea & Febiger, Philadelphia. Price $4.50.

The author has presented to the general practitioner of medicine a very readable story of allergy, in a concise, orderly fashion. He brings an "allergy consciousness" to the reader which will redound to the benefit of many patients who may have been previously relegated to the great and unfortunate group—the neurasthenic.—A.J.B.

MEDICAL CLINICS OF NORTH AMERICA. (Issued serially, one number every other month.) Volume 17, Number 1. (Cleveland Clinic Number—January 1934) Octavo of 253 pages with 53 illustrations. Per Clinic Year July 1933 to May 1934. Paper, $12.00; Cloth, $16.00 net. Phiadelphia and London: W. B. Saunders Company, 1934.

Clinical Factors in the Production of Anemia and the Regeneration of Erythrocytes and Hemoglobin by Russell L. Haden. In this article the author gives the course of the red cell through its production to its destruction; the different abnormalities of the production and of destruction, and lists the laboratory studies necessary, the causes of the various anemias and the treatment.

Dr. Haden has another very excellent article on the study and treatment of chronic arthritis with the presentation of one case and gives an excellent treatise on treatment of these conditions.

Dr. E. Perry McCullagh has a clinic on the management of the parathyroid tetany and the management with and without calsium presenting three cases.

(Continued on Page 195)

THE PRESIDENT'S MESSAGE

To the Members of the Kansas Medical Society:

With so much of our time consumed in trying to keep up with current events, we are inclined to neglect the routine subjects of our profession.

It is possible to develop honest action among our people by proper education. Intelligent action along certain lines can accomplish the desired results. In legislation, for instance, unless we educate people to a better understanding of the requirements of our profession, measures will continue to be proposed and in some cases become laws, which never should have passed had there been an explanation of the seriousness of the matter.

It seems to me our hope lies in wholehearted cooperation within our organization and we, as individuals, should do our part. We should not choose ideals which conflict in any way with our communities, but in our choice should extend our influence in such a way that our purpose will be recognized by those with whom we come in contact.

We are all trying to accumulate material for success, however, let us not lose sight of the unlimited field which our profession offers for helping the unfortunate.

Through intelligent understanding of our purpose to educate the laity for their own good, we may accomplish the hoped for results and the correct solution of our problem.

Yours Fraternally,

W. F. Bowen.

President, Kansas Medical Society

Topeka, Kansas
April 20, 1934

THE JOURNAL
of the
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EDITORIAL

SOME PROBLEMS IN THE TREATMENT OF CANCER

A cancer survey of the State of Kansas has just been completed by the American Society for the Control of Cancer. A report of this survey will be made at the annual state medical society meeting so that every physician in the state may be able to familiarize himself with the entire cancer problem as it exists in his locality.

Cancer stands second as a cause of death in the registration area of the United States and its frequency is increasing. It caused 8.6 per cent of all deaths in the United States in 1930. Even a casual review of the subject will indicate that cancer as a whole is not being treated efficiently, chiefly because it is either not recognized early by the doctor or patient or the importance of early treatment is not clearly appreciated.

To preach about cancer may seem futile to many. Others may assume a fatalistic attitude and brush aside the problem as one not worthy of the effort. To such individuals, attention may be called to the fact that the excellent present day control of tuberculosis was not achieved without effort. For the control of cancer, the second most deadly disease, the public and profession are now receiving the call that was sent out a few years ago to eradicate the ravages of the white plague. This call is being answered by local surveys, education of the public, education of physicians and establishment of cancer clinics. A not unimportant phase of the educational problem is the necessity of a concerted effort to eradicate all quacks and irregular practitioners of medicine who take advantage of a disease being given publicity to prey upon the cupidity of sufferers who are not capable of differentiating between science and sophistry. Hope is the sheet anchor of both the afflicted and the quack and cannot be disregarded in educating the laity concerning the treatment of cancer. The quack always offers hope regardless of honesty. Physicians and patients can best combat the medical parasites by learning to recognize cancer at a stage when the possibility of a cure can with honesty be promised.

The medical profession should take a positive stand in the cancer education of their patients. To do this physicians must have definite and clear cut knowledge of the natural history of cancer as well as what may be expected when proper treatment is given. Every effort should be made to stamp out the very general belief that life is as good as lost

as soon as cancer is diagnosed. If every living person could be convinced that cancer at the proper stage is curable, much would be done for its control. This is the function of the physician and especially the family physician. Our patients cannot be stronger in their convictions concerning the treatment of disease than their doctors.

Three patients, entered the University of Kansas Hospital for cancer of the breast the same week illustrate the urgent necessity of educating both physicians and patients as a part of a campaign to lower the cancer death rate. The first patient, a woman, 45 years of age, consulted her doctor two years ago for a lump in her breast. She was told that it amounted to nothing and tincture of iodine was recommended. She later consulted another physician who told her not to be alarmed unless "lumps" appeared under the arm. The second patient consulted her physician because of a nodule in her breast 18 months ago. Operation was advised and rejected. She is quite religious and chose to trust in the reading of her bible as a means of therapy. The third woman was sent to the hospital by her family doctor for the repair of old perineal and cervical lacerations. She knew she had a mass in her breast but did not tell her doctor. She was sure that the mass which she had noticed eight months before was due to the old lacerations and would be readily cured by their repair. These three patients all have advanced cancer of the breast with involvement of the axillary lymph nodes. It is doubtful if their chances of a ten year cure are more than ten per cent. Certainly education is the only means of correcting such errors as these patients demonstrate.

It must be impressed upon physicians and the public alike that in the present state of scientific knowledge that the only efficient treatments of cancer are surgery (which includes various types of cautery excision or destruction), *x*-ray and radium. Destructive pastes and other chemicals have no place in cancer treatment. Efficient surgical treatment is much more generally available than efficient *x*-ray and radium therapy. The former is more standardized than the latter. *x*-Ray and radium treatments have been rapidly changing in recent years, but are far from being standardized even at the present time. Controversy is still active concerning the efficacy of surgery compared to treatment by radiation. It is unfortunate that there is not as yet a clear cut field for each type of therapy. Since it is well recognized that this is not true the opinion of those that treat cancer best is firm in the conviction that all cancer should be treated as a group problem having available the cooperation of surgeon, radiologist and pathologist.

THOMAS G. ORR, M.D.

THE DEVELOPMENT OF PRE-CLINICAL INSTRUCTION IN BACTERIOLOGY AND IMMUNOLOGY

Although medical education may be traced back into antiquity and anatomical dissection to the early centuries of the Christian era, the remaining laboratory sciences have formed an integral part of the university curriculum for only a little more than a century.

Purkinji established the first university laboratory of physiology in 1824 at Breslau. The first university to establish a chemical laboratory was at Giessen in 1826; Liebig was made director. In 1838 Johannes Müller assumed the directorship of the physiological institute at Berlin and trained Schwann and Virchow who applied Schwann and Schleiden's cellular theory of plant tissue to animal tissues. Virchow established his

first pathological laboratory at Berlin in 1855 and published his final concept of "cellular pathology" in 1858. This is regarded as one of the great contributions of the 19th century.

To appreciate that bacteriology and immunology are relatively new to the medical curriculum one has only to recall that Dr. Welch, now emeritus professor of the history of medicine at Johns Hopkins, was actively engaged in postgraduate work in pathology in Germany (1876-78) before bacteriology and immunology were completely established as laboratory sciences. While Pasteur had explained fermentation, offered ample proof of the "germ theory" of disease and rediscovered the Jennerian principle of active immunization with an attenuated virus, Koch had not as yet introduced solid media or formulated his postulates and the cause of tuberculosis, diphtheria, typhoid fever, bacillary dysentery, tetanus, gas gangrene and most of the infectious diseases were unknown. Koch had made his great contributions and many new organisms had been discovered by the time Welch accepted the chair of pathology at Johns Hopkins in 1884 and Theobald Smith, the position in pathology at George Washington University in 1886. Pasteur and Koch changed the teaching relative to the cause and prevention of infectious diseases.

The next decade saw the beginning of the science of immunology. Toxins (1888-1889) and antitoxins (Behring, 1890) were discovered and the latter was introduced into clinical medicine about 1894. The agglutination test was suggested as a diagnostic procedure by Widal and Gruber (1896) and Bordet immediately explained the mechanisms involved in this and other antigen and antibody reactions from the standpoint of physical chemistry. The concept of cellular immunity was developed in Pasteur's laboratory by Metchnikoff while the German school under the leadership of Pflügge, Ehrlich, Behring and others inaugurated the humoral theory.

During the next decade ending with 1906, many new concepts crept into the preclinical sciences. Bordet and Gengou (1901) suggested the use of complement fixation in diagnoses. Wassermann (1906) applied it to the diagnosis of syphilis after Schaudin (1905) had discovered the etiological factor, *Treponema pallidum*. Landsteiner (1901) discovered the blood groups and during this period he began his remarkable work on modified antigens. Richet (1903) and also Theobald Smith discovered anaphylaxis. Wright in England and Russell in America advocated active immunization against typhoid fever. While it is quite probable that Welch, Theobald Smith, Hektoen, Gay and a few others mentioned these discoveries to their students at the time they were published they did not become an integral part of medical education until the next decade. Between the years 1906 and 1917, the Wassermann test and typhoid immunization came into general use, Moss published on the blood groups (1910) and during the World War compatibility tests and blood transfusion became popular. The Schick test appeared in 1913 and Park began immediately his brilliant work in active immunization against diphtheria, the results of which did not meet with general use until after 1920. Prior to 1918 bacteriologists as a rule had unhesitantly accepted the concept of Cohn (1875) and Koch (1877) that bacterial characteristics such as morphology, fermentative powers, or pathogenicity, are constant and inheritable and that all organisms in a colony or pure culture are alike. Since then largely through the work of Andrews, DeKruiff and others

the concept of bacterial dissociation into smooth and rough variants, the former virulent and the latter nonvirulent has developed and is only recently appreciated. It has been shown that the organism forming the smooth colonies of pneumococci owe their type specificity to complex sugars and that these carbohydrates play a role in infection. Avery and Goebel at the Rockefeller Institute have succeeded in transforming one type of pneumococcus into another, thus at least throwing some doubt upon the concept of constancy of bacterial characters held by Koch. Quite recently it has been shown that swine influenza and perhaps also human influenza are caused by a dual infection of a filterable agent and a rod-like organism belonging to the hemophilic group. Thus the previously held concept that every infectious disease is caused by one specific agent is found to have exceptions.

It is also interesting to note that, judging from the quiet and sympathetic reception given to the views of Hadley of Michigan and Mellon of Pittsburgh on bacterial variation that there is a trend toward more openmindedness or perhaps philosophy in pathogenic bacteriology corresponding in a measure to the change in attitudes noted in physics and chemistry since 1911. During the past decade immunology has become a separate course in the medical curriculum and is being presented as a science rather than a set of empirically performed laboratory exercises. During this time there has occurred great refinement and an incease in number of serological techniques used in diagnosis and of vaccines and serums used in active and passive immunization respectively. These along with the changing concepts as to the nature of bacteria, viruses, red cells, antibodies, local immunity, tissue hypersensitiveness and mechanisms of reactions will form the content of the immunology texts of tomorrow. The lag period between progressive research and academic teaching is a hurdle to be overcome by the medical faculty.

NOBLE P. SHERWOOD, Ph.D., M.D.

EDITORIAL COMMENT

The American Association for the Study of Goiter will hold its annual meeting in Cleveland, June 7-9, 1934.

The University of Wisconsin has just received a bequest of $300,000 from the late Miss Jean Bowman of Wisconsin Dells to found a cancer clinic and research center. *(The Diplomate*, April, 1934).

The Mantoux test was recently given to approximately 6,800 school children in Omaha Nebraska. Positive reactors numbered 1,350, or nearly 20 per cent. No active cases of tuberculosis were found.

It is reported the Louisiana State Board of Medical Registration will in the future require every physician from a foreign medical school to have in addition to a foreign diploma, one from a medical college in the United States and recognized by the board.

Dr. Jay Frank Schamberg, professor of dermatology and syphilology, University of Pennsylvania Graduate School of Medicine, Philadelphia, and director of the Research Institute of Cutaneous Medicine, died March 30, 1934, of heart disease. *(J.A.M.A.*, April 14, 1934).

The Medical Women's National Association will hold its annual meeting in Cleveland on June 10, 1934, just preceding the meeting of the American Medical Association. Headquarters have been established in the Hotel Cleveland. Dr. Elvenor Ernest, of Topeka, is regional director of the Southwest Central District.

The American Medical Golfing Association will hold its twentieth annual tournament at the Mayfield Country Club in Cleveland on June 11, 1934. Thirty-six holes of golf will be played in competition for the 50 trophies and prizes in eight events. Dr. Homer K. Nicoll, of Chicago, is president of the association and William J. Burns, of Detroit, secretary.

THE LABORATORY

Evaluation of Laboratory Service

CECIL G. LEITCH, M.D.*

Clinical and research laboratories have become a fundamental part of the medical instruction of today, and are valuable adjuncts to the practicing physician in handling problems of disease. These columns have from month to month carried well written and carefully selected methods of diagnostic assistance available to the clinician in his local laboratory or in the laboratory of the nearby hospital. Realizing that this laboratory editorial makes available to the reader of this journal the latest procedures of value to the practitioner, I propose to briefly present a review of some medical observations of recent years in the development of which the laboratory has been a potent factor under the direction of many careful investigators.

The developments in the field of vitamine research comprise a most intriguing chapter in recent developments in medicine. With the recognition of fundamental pathological changes resulting from deficiency of the various vitamines and an available source of supply of these vitamines, the diagnosis and treatment of these deficiencies has been made possible. The demonstration of the essential nature of a balanced nutrition in the maintenance of health is, of course, the ultimate goal of these researches.

The diagnosis of anemias and their re-classification has resulted from the perfection of numerous new methods of study of the qualities and characteristics of the red blood cells together with the demonstration of necessary factors in hemoglobin synthesis initiated by the experimental work of Whipple and clinical investigations of Minot and Murphy. The later ramifications of this study preclude further discussion except to mention the recent suggestion of Castle as to the identity of the extensive factor necessary for hemoglobin synthesis which he believes may be a vitamine and which is necessary to bring about the remission in pernicious anemia. Anemias of the secondary type have received no less attention and it is quite clearly shown that a depletion of the essential reserves for hemoglobin synthesis—particularly iron—is a prominent etiological factor. Intrinsic defects in the gastric mucosa play an important role in the development of pernicious anemia and are also of importance in the absorption of iron from the intestinal tract in the hypochromic type of anemia.

Much attention is focused at the present time by clinical laboratory and research investigators upon the leukocytic dyscrasias—particularly the syndrome of agranulocytosis. These studies are directed toward the recognition of the underlying pathology and methods of treatment the most successful of which at present is nucleotid therapy; the assumption being that nucleic acid derivatives exert a direct myelopoetic stimulus. The value of differential counts of white blood cells has received considerable attention especially as concerns their prognostic significance—particular attention being given to lymphocytes and the diseases involving the lymphatic tissues.

The question of virus diseases has received a great deal of attention in recent years with these observations as a result. The work of Kendall with his announcement that he could at will change visible pathogenic organisms into an invisible filter passing form seemed revolutionary, and as yet is not confirmed. The one result of these studies is, however, an increasing realization of the instability of the many bacterial forms under varying environmental conditions. The observations made concerning the ability to prevent poliomyelitis by the use of immune serum, and the finding that normal adult human serum is frequently as effective in passive protection as convalescent serum has been important. It remains questionable, however, as to whether convalescent serum is curative in poliomyelitis if the paralytic stage is reached.

The early diagnosis of pregnancy has been made more feasible by the Fried-

*Director of Clinical Laboratories.

man modification of the Ascheim-Zondek test. Attempts at the determination of sex of the unborn child, though heralded as practical a few months ago, still lacks confirmation.

In attempting to survey the developments in medicine, even in a superficial manner, one is impressed with the extent to which the activities of the laboratory has permeated the field of diagnostic medicine and how indispensable they are in the successful management and control of many diseased conditions.

RECENT MEDICAL LITERATURE

Edited by
WILLIAM C. MENNINGER, M.D., Topeka

FATAL TULAREMIA

These authors report a fatal case and the autopsy findings as well as summarizing from the literature all the fatal cases of tularemia which have come to autopsy. Their general comment is that the pulmonary lesions are the most important feature of the visceral pathology, and the next most frequent site of involvement in the fatal cases reviewed was in the central nervous system. Of the pulmonary lesions described, almost any sort of pathology had been discovered although the most characteristic lesion is a lobular type of pneumonia, containing foci of necrosis.

Fatal Tularemia. Review of Autopsied Cases with a Report of a Fatal Case. Gundry, Louis P., and Warner, C. Gardner. Annals of Internal Medicine 7:837-852. January 1934.

THE ETIOLOGY OF PEPTIC ULCER

This author outlines the various hypotheses concerning the cause of peptic ulcer, including circulatory disturbances, erosion of tissue by acids, neurogenic factors, inflammation and infection, and a discussion of the ulcer diathesis. Then he attempts to apply some of these hypotheses to explain the etiology of peptic ulcer in clinical problems of ulcer in man. His conclusion is that peptic ulcer is a result of several inter-acting and variable factors. He makes very little mention of the psychological factors in gastric ulcer, a subject which is being given a great deal of consideration by both internists and surgeons.

Clinical Considerations of the Etiology of Peptic Ulcer. Rivers, Andrew B. The Archives of Internal Medicine 53:97-119. January 1934.

RECENT ADVANCES IN CARDIOLOGY

These writers make a general summary most of which is rather of a review nature but add the very interesting information from various life insurance companies as to the effect of the depression on heart disease. It is interesting to note that in the information supplied by the Mutual Life Insurance Company of New York angina pectoris jumped from 63 deaths in 1930 to 125 deaths in 1932, and that other diseases of the heart jumped from 234 to 286, having risen to 340 in 1931; and diseases of the arteries increased from 112 to 218 between 1930 and 1932. The writers assume that the additional stress and strain of the depression on the general populace is in some part accounting for this increase in heart disease.

Recent Advances in Cardiology. Bishop, Louis Faugeres, and Bishop, Louis Faugeres, Jr., Clinical Medicine and Surgery. 41:15-17. January 1934.

THE PATHOLOGY OF ABNORMAL UTERINE BLEEDING

This study is a resume from the Department of Obstetrics and Gynecology of the Yale University School of Medicine. The author in a very concise fashion outlines all the possible causes of abnormal uterine bleeding in puberty during the reproductive period both during pregnancy and labor and the puerperium and also in the absence of pregnancy as well as during the period of the menopause. He discusses each of these causes briefly which are herewith listed.

In puberty there is the probable endocrine dysfunction and the association with malignant neoplasms, either sarcoma or carcinoma. During the reproductive period in pregnancy before labor there is the threatened abortion, tubal pregnancy, incomplete abortion, hydatidiform mole, cervical lacerations, and cervical adenoma. Later in labor there is the placenta previa, the premature separation of the normally implanted placenta, and vaginal varicosities, as well as uterine atony, cervical lacerations, and retention of placental tissue. During the puerperium the author lists placental

polyp, subinvolution, uterine myomata, chorioepithelioma. In the absence of pregnancy he lists various adenomata, endometrial hyperplasia, chronic cervicitis, acute or chronic pelvic inflammatory disease, ovarian tumors, and general diseases along with uterine displacements. During the menopause he lists cervical and uterine adenomata, various types of carcinoma and sarcoma and endometrial hyperplasia. All of these subjects are taken up and discussed in some detail in a very excellent paper.

The Pathology of Abnormal Uterine Bleeding. Morse, Arthur H. The Yale Journal of Biology and Medicine, 6:89:100. December 1933.

PERSONALS—NEWS ITEMS

Topeka: Dr. and Mrs. Ralph M. Fellows have returned from a week's motor trip to Danville, Chicago and Salisbury, Missouri.

Kansas City: Dr. C. Omer West addressed the April meeting of the Ford County Medical Society at Dodge City, on "Epidermophytosis."

Topeka: Doctors Arthur D. Gray and Karl A. Menninger addressed the Kansas City Urological Society, Kansas City, Missouri, on March 7.

Kansas City: Dr. W. J. Feehan attended the meetings of the Tulsa County Medical Society, at Tulsa, Oklahoma, April 5-8, 1934, and presented a discussion on "Fractures."

Topeka: Dr. Karl A. Menninger addressed the Third Annual Graduate Educational Meeting of the Indiana State Medical Association at Evansville, on April 26, on "Psychoanalysis and Neuro-Psychiatry."

THE PHYSICIAN'S LIBRARY

(Continued from Page 187)

Dr. Henry J. Johns has an interesting and instructive clinic on hyperinsulinism in which he brings forth a very new and perhaps radical method of treatment.

The Treatment of Digestive Disturbances in Asthenic Patients by Dr. C. L. Hartsock. This is, indeed, a very interesting clinic and should be studied by every one who should have access to it. He divides the cases into four groups, giving the various symptoms and a very careful discussion of their treatment.

Dr. R. H. McDonald gives a very interesting clinic on clinical types of Bright's Disease using Addis' classification. He gives a differentiation between different types presenting three typical cases with complete discussion of each case.—C.K.S.

A DIABETIC MANUAL for the Mutual Use of Doctor and Patient, (Fifth Edition, Revised) by Elliott P. Joslin, M.D., Clinical Professor of Medicine, Harvard Medical School; Medical Director George F. Baker Clinic for Chronic Disease at the New England Deaconess Hospital; Consulting Physician, Boston City Hospital, Boston, Mass. This is a small book 5½" x8"x½", containing 224 pages and 49 illustrations. Published by Lea & Febiger, Philadelphia. Price $2.00.

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cian. It instructs him how to carry out the home treatment. It answers all of the essential questions at the outset concerning food values, diet calculations, danger signs, and the use of insulin, thus saving time and avoiding misunderstandings. This edition covers every advance in the treatment of the disease. It clarifies the doctor's instructions and simplifies diet calculation, another element of the treatment which the patient can do for himself. For these reasons this book is recommended to the laity as well as the profession. In short Joslin's Diabetic Manual should be the physician's first prescription for the diabetic.—J.G.S.

—R—

COUNTY SOCIETY NEWS

ELK COUNTY MEDICAL SOCIETY

The Elk County Medical Society met at the court house, Wednesday April 11, at 7:30 p. m. Mrs. H. S. Giere, Poor Commissioner and Case Supervisor for Elk County, met with the society and explained the workings of the Kansas Emergency Relief Committee and its relation to the problems of the physician in handling the medical end of the county poor.

Members present included: Doctors F. K. Day, Longton; R. C. Hutcheson, Elk Falls; C. E. Shaffer, Moline; R. C. Harner and F. L. DePew, Howard.

F. L. De Pew, M.D., Secretary.

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BIRTHS

Horton: Dr. and Mrs. L. C. Edmonds, March 14, 1934; a daughter, Ann Parish.

Liberal: Dr. and Mrs. Albert L. Hilbig, February 13, 1934; a daughter, Albertiann.

Mankato: Dr. and Mrs. R. E. Bennett, February 24, 1934; a son, Lawrence Clayton.

Salina: Dr. and Mrs. Leo J. Schaefer, February 11, 1934; a son, Joseph Peter.

Topeka: Dr. and Mrs. James T. Hunter, March 2, 1934; a daughter, Carolyn Regina.

Wichita: Dr. and Mrs. Louis S. Roberts, March 9, 1934; a daughter.

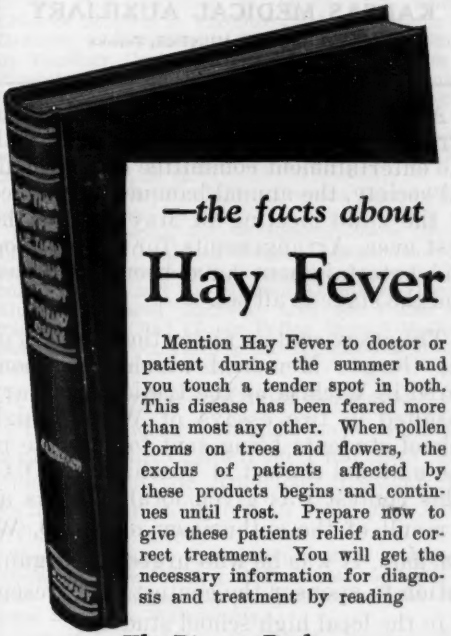
DEATH NOTICES

Brewer, Joseph Francis, Minneapolis, aged 79, died March 11, 1934, of lobar pneumonia. He graduated from University Medical College, Kansas City, Mo., in 1889. He was a member of the Society.

Immel, Albert Allison, Welborn, aged 74, died March 15, 1934, of acute pancreatitis. He graduated from Eclectic Medical University, Kansas City, Mo., in 1913. He was not a member of the Society.

Righter, William Henry, Topeka, aged 81, died April 24, 1934, of hypostatic pneumonia. He graduated from Jefferson Medical College, Philadelphia, in 1879. He was a member of the original faculty of the Kansas Medical College; charter member of the Shawnee County Medical Society, and an emeritus member of the Society.

Scott, Walter Waverly, Kensington, aged 53, died March 18, 1934, of pneumonia. He graduated from University Medical College, Kansas City, Mo., in 1906. He was a member of the Society.



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KANSAS MEDICAL AUXILIARY

MRS. J. THERON HUNTER, Topeka
Chairman of Publicity

According to reports from Mrs. Tihen, Mrs. Friesen, and Mrs. Cox who met with the entertainment committee of the medical society, the annual banquet and dance at the state meeting in May will be the best ever. Arrangements for music, food and entertainment have been completed and the stage is all set.

The essay contest under the auspices of the Gorgas Memorial which was sponsored in Wichita by the Ladies Auxiliary resulted in two essays of Wichita high school students being sent to compete in the national contest at Washington, D. C. This contest was given local impetus as a result of the enthusiasm of Dr. D. W. Basham. It was he who urged the organization to sponsor the contest and present it to the local high school students.

One of the outstanding social meetings of the season in Sedgwick County was held March 19 at the home of Mrs. T. Walker Weaver. All decorations symbolized the arrival of spring. The String Ensemble of Wichita University under the direction of Dean Thurlow Lieurance entertained. Two groups of solos were sung by Mrs. Edna Woolley Lieurance. Rabbi Harry Richmond gave a very interesting talk on "Ancient and Modern Concepts of Art."

The Central Kansas Medical Auxiliary met March 15, 1934, in Hays, at the home of Mrs. Unrein.

The Auxiliary of the Brown County Medical Society met Friday night at the home of the president, Mrs. Paul Conrad. During the business hour matters of interest pertaining to the auxiliary were discussed. Mrs. R. T. Nichols read the news-letter from Mrs. E. J. Nordufth, of Wichita, president of the Kansas Auxiliary. Mrs. W. G. Emery, Mrs. Paul Con-

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rad, and Mrs. R. T. Nichols will represent the Brown County Auxiliary at the state meeting May 10-11 at Wichita. The doctors joined the ladies for an enjoyable social hour. The hostesses assisted by Miss Virginia McDonald served light refreshments. Mrs. Conrad presented each lady with favors of unique Easter novelties. Out of town members attending were Dr. and Mrs. Hibbard, and Dr. and Mrs. Deaver, Sabetha; Dr. and Mrs. McEwen, Morrill.

TRUTH ABOUT MEDICINES

In addition to the articles enumerated in our letter of January 30 the following have been accepted:

Hoffman-La Roche, Inc.—Tablets Digalen-Roche, 1 Cat Unit.

National Drug Co.—Scarlet Fever Streptococcus Toxin for the Dick Test (National) fifty test packages. Typhoid-Paratyphoid A Vaccine, thirty 1 cc. ampule-vials package.

Parke, Davis & Co.—Ortal Sodium. Capsules Ortal Sodium, 3 grains (0.2 Gm.)

Sheffield Farms Co., Inc.—Sheffield B. Acidophilus Milk.

John Wyeth & Brother, Inc.—Ampoule Solution Dextrose 25 Gm. in 50 cc. Ampoule Solution Dextrose 50 Gm. in 100 cc.

Don Baxter Intravenous Products Corporation—Sterile 2½% Dextrose in Physiological Sodium Chloride Solution in Vacoliter Container. Sterile 5% Dextrose in Physiological Sodium Chloride Solution in Vacoliter Container. Sterile 7½% Dextrose in Physiological Sodium Chloride Solution in Vacoliter Container. Sterile 10% Dextrose in Physiological Sodium Chloride Solution in Vacoliter Container.

Eli Lilly & Co.—Solution Liver Extract Concentrated-Lilly Ampoules Solution Liver Extract Concentrated-Lilly, 10 cc.

G. D. Searle & Co.—Tablets Procaine Borate Without Epinephrine.

Sharp & Dohme, Inc.—Antipneumococcic Serum, Types I and II Combined-Mulford. Antipneumococcic Serum, Concentrated (Pneumococcus Antibody Globulin, Types I and II)—Mulford. Diphtheria Toxoid, Alum Precipitated (Refined). Live Oak Pollen Extract-Mulford; Red Clover Pollen Extract-Mulford; Sweet Clover Pollen Extract-Mulford; Southern Ragweed Pollen Extract-Mulford.

New and Nonofficial Remedies

The following products have been accepted by the Council on Pharmacy and Chemistry of the American Medical Association for inclusion in New and Nonofficial Remedies:

Typhoid Vaccine.—This product (New and Nonofficial Remedies, 1933, p. 394) is also marketed in three vial packages (one immunization). The National Drug Co., Philadelphia.

Typhoid-Paratyphoid Combined Vaccine.—This product (New and Nonofficial Remedies, 1933, p. 394) is also marketed in packages of thirty vials (ten immunizations) and in packages of 150 vials (fifty

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immunizations). The National Drug Co., Philadelphia.

Rabies Vaccine-Gilliland.—This product (New and Nonofficial Remedies, 1933, p. 371) is also marketed in packages of fourteen vials, each containing 2 cc. The Gilliland Laboratories, Inc., Marietta, Pa.

Ventriculin, 500 Gm. Bottle.—Each bottle contains Ventriculin (New and Nonofficial Remedies, 1933, p. 264) 500 Gm. Parke, Davis & Co., Detroit, Mich.

Euphthalmine Hydrochloride.—A brand of eucatropine-N.N.R. (New and Nonofficial Remedies, 1933, p. 84). Schering & Glatz, Inc., New York.

Tablets Cod Liver Oil Concentrate-Lederle.—A cod liver oil concentrate in the form of sugar-coated tablets, each containing not less than 1,000 U.S.P. units of vitamin A and not less than 500 A.D.M.A. units of vitamin D. Tablets cod liver oil concentrate-Lederle possess properties similar to those of cod liver oil so far as these depend on the fat soluble vitamin content of the latter. Lederle Laboratories, Inc., Pearl River, New York.

Triethanolamine-Crude.—A mixture containing approximately 75 per cent triethanolamine, 20 per cent diethanolamine, and 5 per cent monoethanolamine. It is an excellent emulsifying agent for use in the preparation of ointments and other dermatologic medicaments. It is claimed to have the power of increasing the penetration of oily substances and to possess a certain amount of bacteriostatic action. (Jour. A.M.A., February 17, 1934, p. 537).

Diphtheria Toxoid, Alum Precipitated (Refined).—Diphtheria Toxoid (Havens). Diphtheria toxin modified by the method of Ramon may be precipitated by the addition of potassium aluminum sulphate. The resultant water insoluble precipitate, which contains the antigenic properties, is purified by washing. Refined diphtheria toxoid, alum precipitated, is used for active immunization against diphtheria. It is administered subcutaneously in one dose.

Refined Diphtheria Toxoid (Alum Precipitated).—Prepared from a seven day culture of the diphtheria bacillus which yields toxin having an L dose of not more than 0.2 cc. The toxin is treated with formaldehyde. The toxoid is precipitated with a solution of alum, washed, and suspended in physiologic solution of sodium chloride to which merthiolate has been added. It is marketed in packages of one 0.5 cc. vial and in packages of one 5 cc. vial, representing one and ten immunizing doses, respectively. The National Drug Co., Philadelphia.

Refined Diphtheria Toxoid Alum Precipitated-Squibb.—Prepared by treating diphtheria toxoid with a solution of alum until complete precipitation is produced. The precipitate is washed and suspended in physiologic solution of sodium chloride. It is marketed in packages of one 0.5 cc. vial and in packages of one 5 cc. vial, representing one and ten immunizing doses, respectively. E. R. Squibb & Sons, New York.

Soluble Gelatine Capsules Parke-Davis Haliver Oil, Plain, 3 Minims.—Each capsule contains Parke-Davis haliver oil, plain (The Journal, November 18, 1933, p. 1634), 3 minims, with sufficient cod liver oil to fill the capsule. Parke, Davis & Co., Detroit. (Jour. A.M.A., February 24, 1934, p. 605).

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Ampules Solution Antimony Sodium Thioglycollate, 0.5 per cent, 10 cc.—Each ampule contains antimony sodium thioglycollate (New and Nonofficial Remedies, 1934, p. 67), 0.5 per cent, 10 cc. Hynson, Westcott & Dunning, Baltimore. (Jour. A.M.A., March 10, 1934, p. 767).

Scarlet Fever Streptococcus Toxin for the Dick Test-National (New and Nonofficial Remedies, 1934, p. 406).—Also marketed in packages of one vial containing sufficient toxin for fifty tests. The National Drug Co., Philadelphia.

Typhoid-Paratyphoid A Vaccine.—This typhoid vaccine (New and Nonofficial Remedies, 1934, p. 401) is also marketed in packages of thirty 1 cc. ampule-vials containing 750 million killed typhoid bacilli and 250 million killed para-typhoid A bacilli per cubic centimeter. The National Drug Co., Philadelphia. (Jour. A.M.A., March 17, 1934, p. 842).

Ortal Sodium.—The monosodium salt of n-hexylethyl barbituric acid. Ortal-sodium differs from soluble barbital, U.S.P. (sodium diethylbarbiturate), in that one of the ethyl groups of the latter is replaced in the former by a n-hexyl group. The actions and uses of ortal sodium are essentially similar to those of barbital, but ortal sodium is more active than barbital and it is used in correspondingly smaller doses. It is marketed in capsules of 3 grains (0.2 Gm.). Parke, Davis & Co., Detroit.

Tablets Digalen-Roche, 1 Cat Unit.—Each tablet contains digalen-Roche (Cloetta) (New and Nonofficial Remedies, 1934, p. 158), 1 cat unit. Hoffman-La Roche, Inc., Nutley, N. J.

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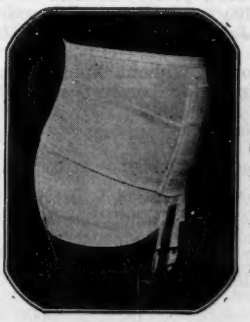

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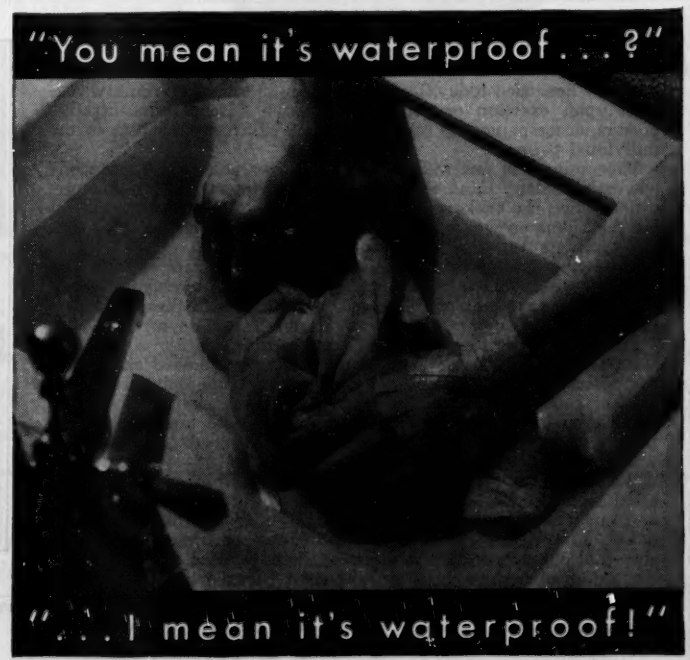

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Ampoule Solution Dextrose 25 Gm. in 50 cc.—Each ampule contains dextrose—U.S.P. (New and Nonofficial Remedies, 1934, p. 270) 25 Gm. in distilled water to make 50 cc.; buffered with sodium citrate 0.25 per cent. John Wyeth & Brother, Inc., Philadelphia.

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Propaganda for Reform

Pertussis Vaccine.—All vaccines of B. pertussis were omitted from New and Nonofficial Remedies in 1931 because no conclusive evidence had been accumulated regarding the therapeutic or prophylactic efficacy of such preparations. The recent work of Dr. Louis W. Sauer (The Journal, January 28, 1933, p. 239, and November 4, 1933, p. 1449) has aroused renewed interest in the subject. Sauer states that preparations made according to his technic are valuable immunizing agents against whopping cough. Eli Lilly & Co. is now manufacturing pertussis vaccine according to the Sauer method. Sauer has presented 394 cases of apparent immunity (beginning three months after inoculation and extending to, and possibly beyond, four years following inoculation) to whooping cough under circumstances ordinarily considered conducive to the spread of the disease. Although Sauer's work appears promising, it is pointed out that the present series of cases is quite limited; the work has been carried on in one locality (where, conceivably, the vaccines used may all have been of the same strain as the current infections), and the past results have been directly contradictory. In view of this the Council does not feel justified, at this time, in recognizing the use of pertussis vaccine of any sort for therapy or prophylaxis until more convincing evidence becomes available. The Council, therefore, postponed consideration of B. pertussis vaccine, Lilly (Sauer method) to await the development of further evidence. (Jour. A.M.A., March 3, 1934, p. 692).

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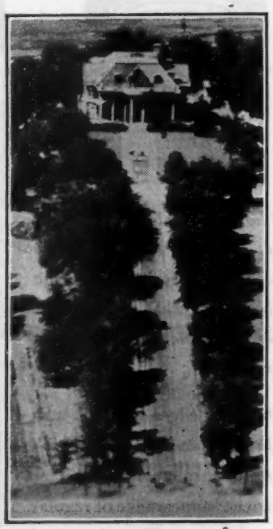
The etiology is not well known or rather, it is somewhat controversial. Many think that over-work is responsible for the condition, when the background of the personality is unstable. Others lay the blame on worry, but some observers believe that the worry is a symptom, rather than a cause of the condition.

The symptoms of this condition occur in many diseases which have a morphological background. Changes in the chemistry and the hormone content of the blood, resulting from these morphological changes, apparently are responsible for the symptoms.

Because of this fact, we have been considering, for some time, the theory that this symptom complex always followed changes in the metabolism, so minor that our rather crude laboratory and clinical approaches, could not determine these changes. We decided to make an empirical approach and, to date, our results have been excellent, although they have not advanced far enough to warrant any positive statements.

We feel that all of these cases must have a thorough study into all the endocrines and all the chemical constituents of the blood, and any change—no matter how slight—must be further investigated. Empirical methods of treatment must be tried when we are sure that our preparation will act as it is advertised. Unfortunately, we cannot always be sure, so care must be used in drawing conclusions.



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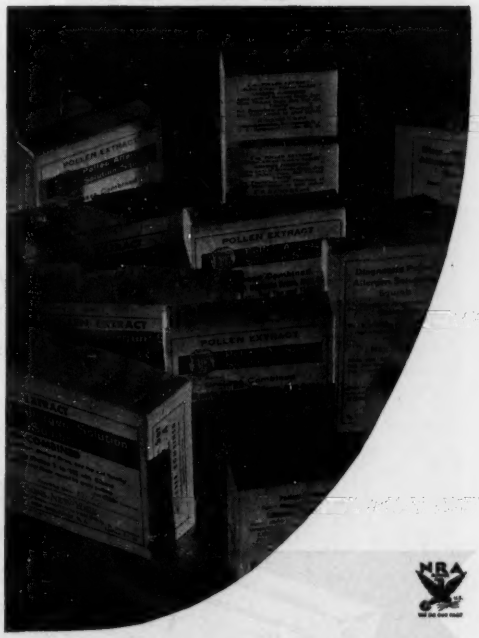

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The absence of clinical symptoms in most cases, leaves a spinal fluid examination as the best available method of diagnosis. Fortunately, this method is dependable and gives essential information for a correct diagnosis.

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Cases of neurosyphilis diagnosed during the incipient stages may be brought under control by the use of Tryparsamide. With the use of Tryparsamide in the early, or meningeal type of case, clinical improvement is prompt in the majority of instances, and serological improvement usually occurs within the first year.

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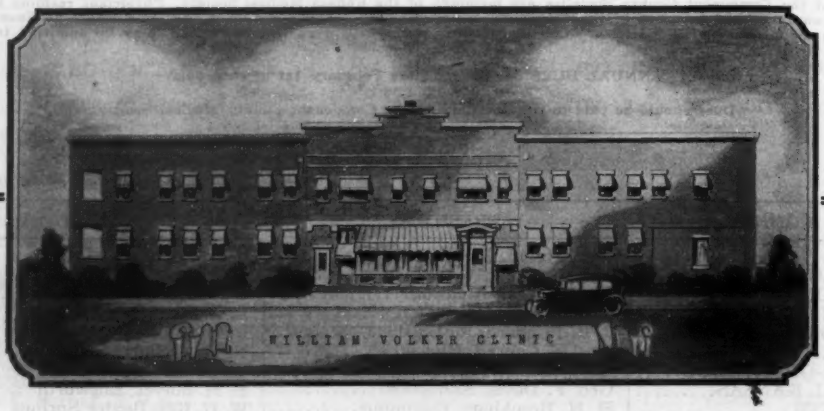

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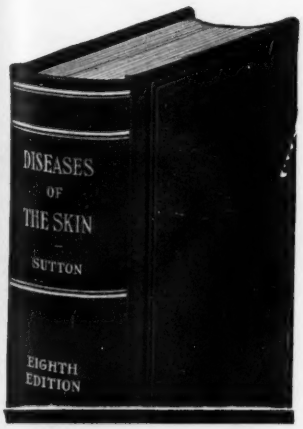

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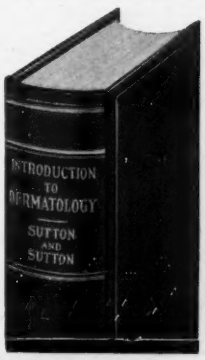

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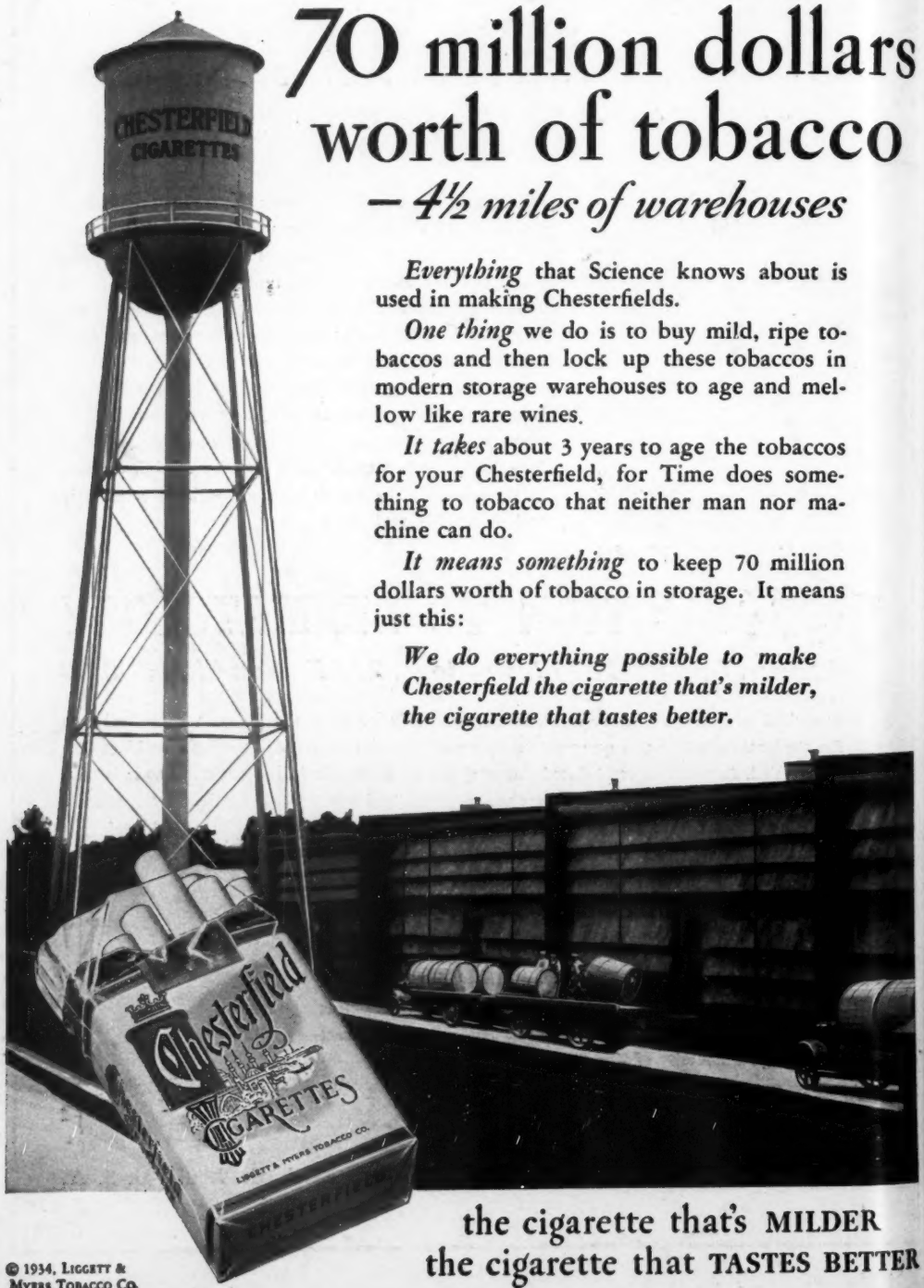

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